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(54) **FIMBRILLIN PROTEIN OF *Si*(PORPHYROMONAS GINGIVALIS)**

(57) A part or the whole of a nucleic acid encoding the fimbriillin protein of *Porphyromonas gingivalis*; an antigen comprising a part or the whole of the above protein; an antibody against the above antigen; and a medicine containing the above antibody. The above acid and antibody are useful for detecting *P. gingivalis*, and the antibody is useful for preventing or ameliorating periodontal diseases.

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Description

TECHNICAL FIELD

5 The present invention relates to fimbrillin, which is the major fimbria structural protein of *Porphyromonas gingivalis* (hereunder referred to as *P. gingivalis*) and fragments thereof, to DNA encoding the fimbrillin, and to fragments thereof. Of such DNA fragments, those with high homology among the bacterial strains are useful for detecting the species, while those with low homology among the bacterial strains are useful as probes for distinguishing between the bacterial strains. Also, the proteins or their fragments which have high homology among the bacterial strains are useful as anti-
 10 gens for the production of antibodies which recognize the above-mentioned bacterial species, while peptides with low homology among the bacterial strains are useful as antigens for producing antibodies capable of distinguishing between the bacterial strains.

The present invention further relates to antibodies with immunoactivity against serum type-common peptide fragments of fimbrillin, the fimbria structural protein of *P. gingivalis*. These antibodies against common peptides may be
 15 used for prevention or improvement of periodontal disease by their common inhibition of fimbria function of different serum types.

BACKGROUND ART

20 *P. gingivalis*, a gram-negative anaerobic bacterial species, has been the focus of attention in recent years as a periodontal pathogenic bacterium, due to its frequent detection in lesions of periodontal patients. The surface layer of the bacteria is known to contain fimbriae which have very high antigenicity. The fimbriae exhibit diverse biological activity against host cells, and are also highly implicated in the pathogenicity of *P. gingivalis*, as an adhesive factor.

The structure of the fimbrial protein is believed to comprise a subunit protein called fimbrillin with a molecular
 25 weight of about 41,000, which is polymerized into some shape.

The only base sequence coding for fimbrillin so far reported is that of *P. gingivalis* strain 381 [J. Bacteriol. 170, 1658 (1988)]. Recently, however, it has become evident that the immunological reactivity of the fimbriae differ among strains [Oral Microbiol. Immunol. 6, 332 (1991)], suggesting that this fimbrial protein is not consistent among *P. gingivalis*
 30 strains.

Thus, it has been a goal to elucidate the genetic sequences coding for fimbrillin of *P. gingivalis* with different immunological reactivities, and clarify the differences between bacterial strains.

However, inhibition of the pathogenicity of *Porphyromonas gingivalis* using antibodies against the fimbriae of the *Porphyromonas gingivalis* with different immunological reactivities requires antibodies against the fimbriae of each serum type, which is not feasible.

35 However, it is believed possible to inhibit fimbrial function through reaction of a single antibody with fimbriae of *Porphyromonas gingivalis* with different immunological reactivities, by using an antibody which is specific to a sequence common to their fimbrillin proteins.

DISCLOSURE OF THE INVENTION

40 It is an object of the present invention, therefore, to provide DNA coding for the fimbrillin proteins of different strains of *P. gingivalis*, DNA fragments with high homology among the bacterial strains which are useful as probes for detecting the above-mentioned species, and DNA fragments with low homology among the bacterial strains (strain-specific) which are useful as probes for distinguishing between strains; as well as fimbrillin proteins from different strains having
 45 specific amino acid sequences, peptides having amino acid sequences with high homology among the bacterial strains which are useful for producing antibodies recognizing the species, and peptides having amino acid sequences with low homology among the bacterial strains (strain-specific) which are useful for producing antibodies capable of distinguishing between strains.

It is a further object of the present invention to provide antibodies capable of commonly reacting with these *Porphy-*
 50 *romonas gingivalis* strains, by using antigens which are peptide fragments selected from amino acid sequence portions with high homology among the amino acid sequences of fimbrillin proteins of *Porphyromonas gingivalis* with different immunological reactivities, or the same peptide fragments bound to suitable proteins.

In order to accomplish the above-mentioned objects, the present invention provides DNA coding for the fimbrillin proteins of *Porphyromonas gingivalis* strains ATCC33277, BH18/10, HW24D-1, OMZ314, OMZ409, ATCC49417, 6/26
 55 and HG564, which are included in the base sequences represented by Sequence Nos. 2 through 9.

The present invention further provides DNA having any base sequence forming a region comprising at least 10 contiguous bases, with at least 50% base sequence homology between at least 2 different base sequences of the base sequences listed as Sequence Nos. 1 through 9.

The present invention further provides DNA having any base sequence forming a region comprising at least 10 contiguous bases, with less than 50% base sequence homology between at least 2 different base sequences of the base sequences listed as Sequence Nos. 1 through 9.

The present invention further provides fimbriin proteins of *Porphyromonas gingivalis* having the amino acid sequences listed as Sequence Nos. 11 through 18.

The present invention further provides a peptide having any amino acid sequence forming a region comprising at least 5 contiguous amino acids, with at least 50% amino acid sequence homology between at least 2 different amino acid sequences of the amino acid sequences listed as Sequence Nos. 10 through 18.

The present invention further provides a peptide having any amino acid sequence forming a region comprising at least 5 continuously linked amino acids, with less than 50% amino acid sequence homology between at least 2 different amino acid sequences of the amino acid sequences listed as Sequence Nos. 10 through 18.

The present invention further provides expression vectors comprising the different DNA described above.

The present invention further provides hosts containing the above-mentioned expression vectors.

The present invention further provides antibodies which react with fimbriin of different strains of *Porphyromonas gingivalis*. Thus, according to the invention, antibodies are produced which react with *Porphyromonas gingivalis* of different serum types, by cloning fimbriin-encoding genes from 9 *Porphyromonas gingivalis* strains, deducing the amino acid sequences for the fimbriins from the base sequences of those genes, comparing the amino acid sequences to discover an amino acid sequence common to the plurality thereof, and preparing an antibody against the peptide having the common amino acid sequence.

The present invention, therefore, relates to antigenic peptides comprising at least 5 linked amino acids selected from the following amino acid sequences which are common to the amino acid sequences for fimbriins of 9 strains of *Porphyromonas gingivalis*:

Sequence (1) Asn (or Lys) Gly Glu Gln Gln Glu Ala Ile
Lys Ser Ala (or Val) Glu Asn Ala Thr (or Ile) Lys Val Glu
Asp (or Asn) Ile Lys Cys Ser (or Gly) (Sequence No.: 21)

Sequence (2) Glu Asp (or Asn) Ile Lys Cys Ser (or Gly)
Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr Gly Ala
(or Glu, Gly) Met Glu (or Lys) Leu Val (or Ala) Gly Lys
Thr Leu Ala (Sequence No: 22)

Sequence (3) Val (or Ala) Gly Lys Thr Leu Ala Glu Val
Lys Ala Leu Thr Thr Glu Leu Thr Ala (or Glu) Glu (or Gly)
Asn Gln Glu Ala Ala Gly Leu Ile Met Thr Ala Glu Pro

(Sequence No.: 23)

Sequence (4) Gln Gly Phe Tyr Val Leu Glu Asn (or Ser)
Thr (or Asp, Lys) Tyr Ala (or Ser, Asp) Gln (or Ala) Asn
(or Ser) (Sequence No.: 24)

Sequence (5) Gly (or Pro) Thr (or Lys) Thr Tyr Tyr Pro
Val Leu Val Asn Phe (or Tyr) Asn (or Glu, Asp) Ser (or
Gly) Asn Asn (or Gly) Tyr Thr (or Ile) Tyr (Sequence No.:
25)

Sequence (6) Ser Asn Asn Tyr Thr Tyr Asp Ser (or Asn)
Asn (or Gly) Tyr Thr Pro Lys Asn Lys Ile Glu Arg Asn His
Lys Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly Thr Asn
(Sequence No.: 26)

Sequence (7) Ile Thr Gly Pro Gly Thr Asn Asn (or Thr)
Pro Glu Asn Pro Ile (or Gln) Thr Glu Ser Ala His (or Asn)
Leu Asn Val Gln Cys Thr Val Ala Glu Trp Val Leu Val Gly
Gln Asn Ala Thr Trp (Sequence No.: 27)

Sequence (8) Thr Gly Ser Leu Thr Thr (or Asn) Phe Asn
Gly Ala Tyr Ser (or Thr) Pro Ala Asn Tyr Thr (or Ala)
(Sequence No.: 28)

The present invention further relates to antigens which are the above-mentioned peptides or carrier/protein complexes.

The present invention further relates to antibodies against the above-mentioned antigenic peptides or antigen complexes, and this encompasses both polyclonal antibodies and monoclonal antibodies.

The present invention further relates to an agent for the prevention or improvement of periodontal diseases which contains any of the above-mentioned antibodies.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a sequence list aligning the mutually corresponding parts of the base sequences of the genes coding for fimbriins of the 9 strains of *P. gingivalis*. The underlined portions indicate the PCR primer sequence. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

Fig. 2 is a sequence list aligning the mutually corresponding parts of the base sequences of the genes coding for fimbriins of the 9 strains of *P. gingivalis*. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

Fig. 3 is a sequence list aligning the mutually corresponding parts of the base sequences of the genes coding for fimbriins of the 9 strains of *P. gingivalis*. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

Fig. 4 is a sequence list aligning the mutually corresponding parts of the base sequences of the genes coding for fimbriins of the 9 strains of *P. gingivalis*. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

Fig. 5 is a sequence list aligning the mutually corresponding parts of the base sequences of the genes coding for fimbrillins of the 9 strains of *P. gingivalis*. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

Fig. 6 is a sequence list aligning the mutually corresponding parts of the base sequences of the genes coding for fimbrillins of the 9 strains of *P. gingivalis*. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

Fig. 7 is a sequence list aligning the mutually corresponding parts of the base sequences of the genes coding for fimbrillins of the 9 strains of *P. gingivalis*. The underlined portions indicate the PCR primer sequence. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

Fig. 8 is a sequence list aligning the mutually corresponding parts of the amino acids sequences of fimbrillins of the 9 strains of *P. gingivalis*. The underlined portions indicate the position of the signal peptide. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

Fig. 9 is a sequence list aligning the mutually corresponding parts of the amino acids sequences of fimbrillins of the 9 strains of *P. gingivalis*. The sites indicated by the colon ":" are the same in all 9 strains, and "-" indicates gaps produced to obtain the best matching position.

DETAILED DESCRIPTION OF THE INVENTION

The present invention first provides novel DNA encoding fimbrillin proteins of different strains of *P. gingivalis*, and novel fimbrillin proteins encoded by the DNA.

According to the invention, *P. gingivalis* strains 381, ATCC33277, BH18/10, HW24D-1, OMZ314, OMZ409, ATCC49417, 6/26 and HG564 are used, chromosomal DNA from these 9 strains is purified from the bacteria and used as templates in the PCR (polymerase chain reaction) to amplify DNA containing the genes (*fimA*) coding for fimbrillin. The amplified *fimA* genes from these 9 strains are cloned, and their base sequences and amino acid sequences are determined.

As a more detailed explanation of the invention, the chromosomal DNA from *P. gingivalis* may be obtained by extraction and purification from cultured cells, etc. The chromosomal DNA is used as the template in the PCR to amplify the DNA containing the *fimA* gene. The PCR primer used is an oligonucleotide of appropriate length synthesized and purified with a DNA synthesizer based on the DNA sequence of the already publicly known *P. gingivalis* 381 *fimA* gene. Here, a restriction endonuclease-recognizing sequence not present in the *fimA* gene is preferably artificially added to facilitate cloning of the amplified PCR product in a vector plasmid.

After digesting the DNA amplified in this manner with the restriction endonuclease added to the primer, DNA ligase may be used to link it downstream of the promoter of a suitable expression vector which has been digested with the same enzyme, and this recombinant DNA may be introduced into *E. coli* or the like to obtain the desired clone. Here, a vector system which allows modification of expression of the protein encoded by the inserted gene is preferably used, such as one including the repressor for the promoter of an expression vector such as *lacI^q*, in either or both the plasmid vector and the DNA of the *E. coli* host.

In order to obtain the desired clones from the transformant obtained in this manner, screening may be performed by a method such as colony hybridization, using the *fimA* gene or a fragment thereof labelled with a suitable compound as the probe.

Also, it may be determined whether or not the obtained clones are the desired ones by extracting and separating the plasmid DNA from the transformed strains, digesting it with a suitable restriction enzyme and then identifying it by agarose gel electrophoresis.

It is even more reliable to confirm expression of the recombinant fimbrillin with a method such as Western blotting using anti-*P. gingivalis* fimbria antibody, after the *E. coli* clones have been induced to express the recombinant proteins.

The base sequences of the *P. gingivalis* *fimA* genes cloned in this manner may be determined in the same manner as described above, by digestion with a suitable restriction enzyme followed by incorporation of a suitable vector, preparation of deletion mutant strains based on the method of Steven Henikoff, extraction and purification of plasmid DNA from the series of deletion mutants, or infection with a suitable helper phage and purification of the single-stranded DNA, and then determination of the base sequence based on the Sanger method.

The results of determining the base sequences are shown as Sequence Nos. 1 to 9. Sequence No. 1 shows the base sequence of a DNA fragment containing the base sequence coding for fimbrillin of strain 381, Sequence No. 2 for that of strain ATCC33277, Sequence No. 3 for that of strain BH18/10, Sequence No. 4 for that of strain HW24D-1, Sequence No. 5 for that of strain OMZ314, Sequence No. 6 for that of strain OMZ409, Sequence No. 7 for that of strain ATCC49417, Sequence No. 8 for that of strain 6/26 and Sequence No. 9 for that of strain HG564.

In addition, the amino acid sequences encoded by the reading frames of these base sequences are shown in Sequence Nos. 10 to 18. That is, Sequence No. 10 shows the amino acid sequence for fimbrillin of strain 381, Sequence No. 11 for that of strain ATCC33277, sequence No. 12 for that of strain BH18/10, Sequence No. 13 for that of strain HW24D-1, Sequence No. 14 for that of strain OMZ314, Sequence No. 15 for that of strain OMZ409, Sequence

No. 16 for that of strain ATCC49417, Sequence No. 17 for that of strain 6/26 and Sequence No. 18 for that of strain HG564.

When the present invention is applied for the identification of *P. gingivalis* or a strain thereof, one of the base sequences listed as Sequence Nos. 1 to 9 or a fragment thereof, of DNA having a substantially identical base sequence, is preferred. Here, "substantially identical" means a sequence which is homologous enough with any of the above-mentioned base sequences so as to be able to distinguish the type or strain of interest. However, the DNA used for production of the fimbriin protein or partial peptide thereof by recombination may have any desired codons coding for the amino acid sequences listed as Sequence Nos. 10 to 18 or portions thereof.

The above-mentioned DNA or fragment thereof is obtained by cloning from the different strains mentioned above, with cleavage or modification, as necessary. Once the base sequence has been determined, however, the desired DNA may be chemically synthesized according to a well-known method. The DNA of the invention may thus be obtained even if the above-mentioned strains are not available.

According to one embodiment of the present invention, a DNA fragment forming a region with high homology among the aforementioned plurality of base sequences may be used as a probe for detection of *P. gingivalis*. Such a DNA fragment may be a DNA fragment in a region comprising at least 10 contiguous bases having at least 50% homology between any 2 different base sequences of the above-mentioned 9 base sequences. The homology is preferably at least 70%, more preferably at least 80% and most preferably at least 90%. The homologous region preferably consists of 20 bases or more.

Such a homologous region may be easily determined by observation of the aligned base sequences, or using an available computer program. According to the invention, "homology" is defined as the ratio of the number of identical bases or amino acids between two different sequences with respect to their total number of bases or amino acids, upon comparison of the base sequences or amino acid sequences of given corresponding regions of the two base sequences or amino acid sequences.

According to another embodiment of the invention, there are provided DNA fragments consisting of regions with low homology among a plurality of base sequences, i.e. with high strain specificity. Such DNA fragments are useful as probes for distinguishing strains belonging to *P. gingivalis*. Such a DNA fragment may be a DNA fragment consisting of a base sequence of at least 10 contiguous bases having less than 50% homology between any 2 different base sequences of the base sequences listed as Sequence Nos. 1 to 9. The homology is preferably 40% or less, more preferably 30% or less and most preferably 20% or less. The length of the continuous non-homologous base sequence is preferably 20 bases or more.

The DNA used as the probe is preferably labelled with commonly used labelling such as radioactive labelling, fluorescent labelling or enzyme labelling. Labelling types, labelling methods and labelling detection methods are a well-known technology in this field.

The present invention further provides peptides having amino acid sequences forming regions with high homology among a plurality of the amino acid sequences listed as Sequence Nos. 10 to 18. Such peptides are useful as antigens for production of antibodies, for example, polyclonal or monoclonal antibodies, which recognize fimbriin of *P. gingivalis*.

Such a peptide may be a peptide with an amino acid sequence of at least 5 contiguous amino acids having at least 50% homology between any 2 different amino acid sequences of the amino acid sequences listed as Sequence Nos. 10 to 18. The sequence preferably has at least 70%, and more preferably at least 90% homology. The length of the continuous amino acid sequence is preferably 10 amino acids or more.

The present invention further provides peptides consisting of amino acid sequences in regions with low homology among a plurality of the amino acid sequences listed as Sequence Nos. 10 to 18, i.e. with high strain specificity. Such peptides are useful as antigens for production of antibodies, i.e. polyclonal or monoclonal antibodies, capable of distinguishing fimbriin of different *P. gingivalis* strains. Such a peptide may be a peptide in a region consisting of at least 5 contiguous amino acids with less than 50% homology between any 2 different amino acid sequences of the amino acid sequences listed as Sequence Nos. 10 to 18. The homology is preferably 40% or less, and more preferably 30% or less.

These peptides are useful as antigens for producing polyclonal or monoclonal antibodies by common methods, and may be used by themselves or bound with other proteins. For example, one of the above-mentioned proteins or peptides may be used as an antigen, either alone or coupled with another protein, for immunization of a suitable mammal or bird, to obtain a fimbriin-specific antibody. The antibody may then be labelled with a suitable labelling compound in the same manner as the oligonucleotide primer described earlier, and used to detect a specific *P. gingivalis*.

Such polypeptides or their coupled forms with proteins such as BSA may themselves be used as vaccine antigens, or the specific antibodies as immunoactive antibodies, for the prevention or curing of periodontal diseases caused by *P. gingivalis*.

A protein or peptide having an amino acid sequence as described above may be prepared by a commonly employed gene recombinant method, or by a common method of chemical synthesis. Thus, the present invention also provides expression vectors comprising the above-mentioned DNA, hosts transformed by those expression vectors, and a method of producing desired protein kinases using those hosts. Therefore, both prokaryotic and eukaryotic hosts may be used.

Prokaryotic hosts which may be used include bacteria, for example *Escherichia coli* and *Bacillus* microorganisms such as *Bacillus subtilis*. The eukaryotic host may be a lower eukaryote, for example yeast including *Saccharomyces* yeast, such as *Saccharomyces cerevisiae*.

Animal cells may be used as higher eukaryotic hosts, for example CHO cells, Hela cells and COS cells. Insect cells such as silk worm cells or Mamestra cells may also be used. Insect imagoes may be used, as well.

The expression vector used may be a plasmid, phagmid, phage or virus, depending on the host. For example, plasmids or phagmids are used for bacterial hosts, plasmids are used for yeast hosts, and viruses such as vaccinia virus or baculovirus are used for animal or insect cells.

The expression vector includes, in addition to the structural gene coding for the above-mentioned protein kinase, expression regulating regions which are operably linked to the structural gene, for example a promoter, enhancer, terminator, etc. Examples of promoters used for bacteria are tryptophan operon, Tac promoter and Trc promoter; examples of promoters used for yeast are TDH₃ promoter, ADHI promoter, GALI-7 promoter and PGKL promoter; examples of promoters used for animal cells are SV40 promoter, Ad2 promoter and vaccinia 75K promoter; and an example of a promoter used for insect cells is polyhedrin promoter.

The culturing of the transformed host and expression of the desired gene may be carried out by common methods depending on which host, promoter, etc. is used. Also, the isolation and purification of the desired protein from the cultured product may be accomplished by an appropriate combination of common methods for isolation and purification of proteins, such as filtration, centrifugation, salting out, column chromatography, electrophoresis, affinity chromatography, and the like.

The detection of *P. gingivalis* using a DNA or peptide according to the invention may be accomplished, for example, in the following manner.

Detection of desired strain using DNA probe

Detection of a desired strain in a test sample may be accomplished by immobilizing a DNA sample, which has undergone suitable treatment, on a nylon membrane or other support and hybridizing it with a DNA probe already labelled with a labelling compound which is suitable to the purpose, and after removing the non-specifically binding labelled DNA probe, detecting the DNA probe.

The DNA probe used here may be one which has been cloned from *P. gingivalis* chromosomal DNA and digested with a suitable restriction endonuclease, or one which has been chemically synthesized with a DNA synthesizer.

The method of labelling the DNA probe may be, for example, the method according Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press (1989) using a radioactive compound such as ³²P, or according to Nucl. Acids Res. 14, 6115 (1986) using alkaline phosphatase.

The general method for detecting the probe may be by autoradiography, coloration reaction, etc., and quantitative detection of the desired strain is also possible by detecting the probe bound to the DNA of the desired strain.

Detection of desired strain using specific antibody

Detection of a desired strain using an antibody specific to the fimbrillin or constituent peptide thereof is possible by employing the general detection method for antigens based on antigen-antibody reaction.

Examples of methods which may be used include the ELISA method, latex agglutination method, immunoelectrophoresis method, Ouchterlony method, etc. The test samples used in these methods may be reacted after pretreatment by heating, etc. either directly or in a suitable solvent, and the amount of the resulting antigen-antibody complex may be directly or indirectly quantitated for quantitation of the desired strain.

In order to obtain an antibody which reacts with fimbrillin proteins of different strains of *Porphyromonas gingivalis*, it is necessary to obtain an antibody against a peptide with an amino acid sequence common to those fimbrillin proteins. Upon comparing the amino acid sequences deduced from DNA coding for fimbrillin proteins of 9 different cloned strains according to the invention, the following 8 representative common sequences were found to exist.

Sequence (1) Asn (or Lys) Gly Glu Gln Gln Glu Ala Ile
Lys Ser Ala (or Val) Glu Asn Ala Thr (or Ile) Lys Val Glu
Asp (or Asn) Ile Lys Cys Ser (or Gly) (Sequence No.: 21)

Sequence (2) Glu Asp (or Asn) Ile Lys Cys Ser (or Gly)
Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr Gly Ala
(or Glu, Gly) Met Glu (or Lys) Leu Val (or Ala) Gly Lys
Thr Leu Ala (Sequence No: 22)

Sequence (3) Val (or Ala) Gly Lys Thr Leu Ala Glu Val
Lys Ala Leu Thr Thr Glu Leu Thr Ala (or Glu) Glu (or Gly)
Asn Gln Glu Ala Ala Gly Leu Ile Met Thr Ala Glu Pro
(Sequence No: 23)

Sequence (4) Gln Gly Phe Tyr Val Leu Glu Asn (or Ser)
Thr (or Asp, Lys) Tyr Ala (or Ser, Asp) Gln (or Ala) Asn
(or Ser) (Sequence No.: 24)

Sequence (5) Gly (or Pro) Thr (or Lys) Thr Tyr Tyr Pro
Val Leu Val Asn Phe (or Tyr) Asn (or Glu, Asp) Ser (or
Gly) Asn Asn (or Gly) Tyr Thr (or Ile) Tyr (Sequence No.:
25)

Sequence (6) Ser Asn Asn Tyr Thr Tyr Asp Ser (or Asn)
Asn (or Gly) Tyr Thr Pro Lys Asn Lys Ile Glu Arg Asn His
Lys Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly Thr Asn
(Sequence No.: 26)

Sequence (7) Ile Thr Gly Pro Gly Thr Asn Asn (or Thr)
Pro Glu Asn Pro Ile (or Gln) Thr Glu Ser Ala His (or Asn)
Leu Asn Val Gln Cys Thr Val Ala Glu Trp Val Leu Val Gly
Gln Asn Ala Thr Trp (Sequence No.: 27)

Sequence (8) Thr Gly Ser Leu Thr Thr (or Asn) Phe Asn
Gly Ala Tyr Ser (or Thr) Pro Ala Asn Tyr Thr (or Ala)
(Sequence No.: 28)

The positions of the amino acid sequences of the above-mentioned Sequence Nos. 21 to 28 in the amino acid
sequences listed as Sequence Nos. 10 to 18 are as shown in the following table.

Table 1

Sequence No.	21	22	23	24	25	26	27	28
Sequence No.								
10	20-42	37-65	60-90	210-222	262-279	274-307	301-337	177-190
11	20-42	37-65	60-90	210-222	262-279	275-307	301-337	177-190
12	20-42	37-65	60-90	210-222	262-279	274-307	301-337	177-190
13	18-40	35-63	58-88	209-221	263-280	275-308	302-338	176-189
14	18-40	35-63	58-88	209-221	263-280	275-308	302-337	176-189
15	18-40	35-63	58-88	209-221	263-280	276-308	302-338	176-189
16	20-42	37-65	60-90	211-223	265-282	278-310	304-(324)	178-191
17	20-42	37-65	60-90	(214)-226	268-285	280-313	306-(327)	178-191
18	-	-	-	(216)-227	267-284	-	307-319	

The antigen peptides of the present invention are peptides comprising at least 5 contiguous amino acids of the above-mentioned amino acid sequences (Sequence Nos. 21-28). The other common peptides shown in Figs. 8 and 9 may also be used in the same manner. In cases where the peptides lack antigenicity due to short length, etc., they may be used as antigens by attachment to a carrier protein.

These peptides may be synthesized by common methods such as the solid phase method or liquid phase method. Alternatively, the peptides may be produced by expression of their encoding genes. The genes may be chemically synthesized or the DNA coding for the amino acid sequences listed as Sequence Nos. 10 to 18 or DNA having, for example, the base sequences listed as Sequences Nos. 1 to 9 may be used as templates to amplify a desired portion thereof by the PCR method. For amplification by PCR, the cleavage site of a restriction endonuclease is preferably bound artificially to the PCR primer.

These DNA themselves may be expressed to obtain the peptides, or they may be linked to DNA coding for other proteins and expressed to obtain fused proteins with other proteins. Such expression may be carried out by common methods.

The desired peptide or fused protein which is obtained in this manner may be used as an immunogen either alone or in the form of a complex with a suitable carrier protein. The type of carrier protein used here may be bovine serum albumin, egg albumin, myoglobin, tetanus toxoid, KLH (keyhole limpet hemocyanin), etc.

Also, the binding of the carrier protein to the peptide of interest may be accomplished using publicly known means. The reagent used for the binding may be, for example, glutaraldehyde, a bis-imido ester, bis-diazotized benzidine, soluble carbodiimide, m-maleimidobenzoyl-N-hydroxysuccinimide, or the like. The binding ratio (molar ratio) of the carrier protein to the peptide is preferably between 1:1 and 1:40, and especially between 1:5 and 1:20.

To obtain polyclonal antibodies, the immunogen obtained in this manner may be used to immunize a mammalian animal (sheep, goat, cow, horse, pig, rabbit, rat, mouse, guinea pig, etc.) or bird (chicken, dove, quail, duck, goose, etc.), and the antibodies obtained from the animal's serum, milk, ova, egg yolk, etc. Mammalian animals may be immunized by a normal method such as subcutaneous, intramuscular or intraabdominal administration of the obtained immunogen, or by nosedrops or eyedrops. If necessary it may be used for immunization in admixture with an adjuvant such as Freund's complete adjuvant. Here, the amount of antigen used per immunization is preferably 0.1-3 mg/kg body weight, and particularly 0.25-2 mg/kg body weight, but an appropriate amount may be selected which gives the desired antibody titer while not adversely affecting the animal.

The immunization may be carried out 3-5 times every 2 to 4 weeks, taking blood from the immunized animal by a common method at 10 to 14 days after the final immunization, to obtain antiserum. The obtained antiserum may be used directly or after treatment by an appropriate process such as salting out, dialysis, ion exchange chromatography, gel filtration, affinity chromatography, etc. to purify the desired immunoglobulin.

Also, though there are no particular restrictions on the bird used for immunization, egg-laying species such as white leghorn hens are preferred from the standpoint of antibody production. The method of administering the immunogen may be the same as described above for mammalian animals, and an appropriate antigen dosage may be selected which gives the desired antibody titer while not adversely affecting the animal. If necessary, it may also be used for immunization in admixture with an adjuvant such as Freund's complete adjuvant.

Antibodies may usually be prepared from a bird immunized in this manner by extraction and separation of immunoglobulin contained in the egg yolk. The method used for the extraction and separation may be a commonly used method of extracting immunoglobulin, such as precipitation using polysaccharides or polyethylene glycol, or extraction using an organic solvent such as ethanol or chloroform, and purification may be accomplished using the method of purification from antiserum described above.

The antibodies may also be obtained and used as monoclonal antibodies. To obtain monoclonal antibodies, the aforementioned immunogen is preferably used to immunize an animal such as a mouse, rat, guinea pig, etc. by a similar method, extracting spleen cells at 2 to 5 days after the final immunization, and preparing monoclonal antibody-producing hybridomas according to a common method. The antibody-producing hybridomas obtained in this manner may be cultured in a suitable medium and monoclonal antibodies may be purified for use from the resulting culture supernatant using the same means as in the aforementioned method of purifying polyclonal antibodies.

The antiserum or antibody titer may be measured using the ELISA method or radioimmunoassay method which are usually employed.

The antiserum, polyclonal antibodies or monoclonal antibodies obtained in this manner react specifically with fimbriae on the surface layer of *Porphyromonas gingivalis*, and thus are immunoactive against *Porphyromonas gingivalis*. That is, the antibodies themselves, or the antibodies labelled with a suitable labelling compound, may be used to specifically detect *P. gingivalis*. The antibodies also have an effect of inhibiting adhesion of *Porphyromonas gingivalis* to intraoral tissue, and thus applying the antibodies intraorally will inhibit intraoral colonization by *Porphyromonas gingivalis* and help prevent periodontal diseases.

Thus, the antibodies according to the invention may be suitably used as active ingredients of prophylactic agents for periodontal disease, and may be combined with various formulations depending on the mode of administration to the oral cavity, for example, dental cream, liquid dentifrice, mouthwash, etc. Other additional publicly known active ingredients may also be combined with the prophylactic agent for periodontal disease according to the invention in addition to the above-mentioned antibodies, depending on the type of formulation.

EXAMPLES

The present invention will now be explained in more detail by way of the following examples.

Example 1: Cloning of DNA coding for fimbrillin protein

Preparation of *P. gingivalis* chromosomal DNA

P. gingivalis strains 381, ATCC33277, BH18/10, HW24D1, OMZ314, OMZ409, ATCC49417, 6/26 and HG564 were anaerobically cultured for 2 days at 37°C in a GAM liquid medium containing hemin and menadione, and the cells collected from centrifugation were washed with a TE buffer (10 mM Tris • HCl, 1 mM EDTA; pH 8.0) and then dispersed in 20 ml of the same buffer.

To this was added 0.4 ml of diethyl pyrocarbonate and heating was conducted at 50°C for 1 hour, after which the cells were again collected by centrifugation and dispersed in 5 ml of a TEN buffer (10 mM Tris • HCl, 1 mM EDTA, 100 mM NaCl; pH 8.0), and then the cells were lysed by addition of lysozyme, SDS and N-lauroylsarcosine sodium to final concentrations of 1 mg, 10 mM and 2%, respectively. Next, proteinase K was added to 50 µg/ml and the mixture was heated at 55°C for one hour. The supernatant obtained from centrifugation was subjected to cesium chloride density gradient centrifugation to separate the chromosomal DNA which was then purified by dialysis against TE buffer.

Amplification of fimA gene by PCR

The obtained *P. gingivalis* chromosomal DNA was used as a template for amplification of the *fimA* gene by PCR. That is, using the base sequence of the *fimA* gene of *P. gingivalis* strain 381 as the basis for the design, primers with the *Bam*HI recognition site (underlined) added [5'-AATTGGATCCGCAGCAAGGCCAGCCCGG-3' (Sequence No.: 19) and 5'-AGAGGATCCGAGCGAACCCGCTCCCTGT-3' (Sequence No.: 20)] were used for 20-30 cycles of PCR with *Taq* DNA polymerase, to amplify DNA containing the *fimA* gene.

Cloning of *fimA* gene

After the DNA amplified by PCR and the expression vector pTrc99 were digested with *Bam*HI, T4 DNA ligase was used for linking. The resulting recombinant DNA was introduced into *E. coli* JM109 which was then cultured overnight on an LB (Luria-Bertani) agar medium containing 100 µg/ml ampicillin to obtain transformant strains.

Screening of positive clones by colony hybridization

After transferring the transformant colonies onto a nylon membrane, the cells were lysed with SDS in the presence of an alkali, and then the ³²P-labelled fimA gene was used as a probe for colony hybridization to screen for the desired positive clones.

Example 2: Expression of recombinant protein by Western blotting

In order to more absolutely confirm that the obtained clones were the desired ones, expression of the recombinant fimbrillin protein was confirmed by Western immunoblot. That is, the *E. coli* clones were shake cultured in LB liquid medium containing 100 µg/ml ampicillin until the OD₅₅₀ reached about 0.3-0.5, and then IPTG was added to 0.2-1 mM and culturing was continued for another hour or more. After the culturing, the cells were collected by centrifugation and subjected to SDS-PAGE, and Western blotting using anti-*P. gingivalis* fimbrillin serum confirmed expression of the recombinant protein at the position of approximate molecular weight 43,000-48,000.

Example 3: Determination of fimA gene base sequence

A DNA fragment containing fimA was digested with BamHI from the desired plasmid DNA, purified, and linked to vector pUC119 using T4 DNA ligase. Two types were prepared, with insertion of the fimA gene in both the forward and reverse directions with respect to the lac promoter of pUC119, and after digestion with KpnI and SmaI, the methods of Steven Henikoff and Yanisch Perron, et al. were basically followed to prepare deletion mutant strains with sizes differing by 100-200 bp each, which were transformed in *E. coli* MV1184 as a series of clones.

The series of defective plasmids were extracted, purified and denatured from the *E. coli* clones, and after infecting the clones with M13 helper phage and extraction and purification of the single-stranded DNA, the base sequences of the fimA genes were determined by the Sanger method.

The sequences of fimA genes of 9 *P. gingivalis* strains were thus elucidated (Sequence Nos. 1-9). From these results, it was found that the DNA base sequences shown in the sequence list had GTG as the initiation codon at bases 216-218 of *P. gingivalis* strains 381, ATCC33277, BH18/10, OMZ409 and ATCC49417, at bases 211-213 of strains HW24D-1, OMZ314 and 6/26 and at bases 187-189 of strain HG564, and coded for the amino acids of Sequence Nos. 10-18 containing the signal sequence.

Example 4: Preparation of antigenPreparation of desired peptides

Among the amino acid sequences of the above-mentioned 9 strains selected as amino acid sequence portions common to the fimbrillin proteins of the different *Porphyromonas gingivalis* strains, the following 4 different desired peptides (1) to (4):

- (1) The amino acid sequence corresponding to amino acids 14-31 of Sequence No. 23 (amino acids 73-89 of Sequence No. 10) (Sequence No. 29): Glu Leu Thr Ala Glu Asn Gln Glu Ala Ala Gly Leu Ile Met Thr Ala Glu Pro
- (2) The amino acid sequence corresponding to amino acids 2-15 of Sequence No. 28 (amino acids 177-190 of Sequence No. 10) (Sequence No. 30): Gly Ser Leu Thr Thr Phe Asn Gly Ala Tyr Ser Pro Ala Asn
- (3) The amino acid sequence corresponding to amino acids 3-17 of Sequence No. 25 (amino acids 264-278 of Sequence No. 10) (Sequence No. 31): Thr Tyr Tyr Pro Val Leu Val Asn Phe Asn Ser Asn Asn Tyr Thr
- (4) The amino acid sequence corresponding to amino acids 4-20 of Sequence No. 27 (amino acids 304-320 of Sequence No. 10) (Sequence No. 32): Pro Gly Thr Asn Asn Pro Glu Asn Pro Ile Thr Glu Ser Ala His Leu Asn were chemically synthesized according to a common method of solid phase synthesis using an automatic peptide synthesizer (product of Applied Biochemicals Co.), and then separated off by high performance liquid chromatography and desalted and purified by gel-filtration.

By another method, DNA coding for the amino acid sequences of the desired peptides were amplified from chromosomal DNA by the PCR, and were introduced into suitable expression vectors and expressed. That is, PCR primers were designed from the desired DNA sequences. The BamHI site was artificially added to the forward primer and the EcoRI site to the reverse primer, with the synthesis performed using a DNA synthesizer.

These PCR primers were used for 30 cycles of PCR with the *Porphyromonas gingivalis* chromosomal DNA as the template, to obtain DNA fragments amplified by common methods. After digestion with BamHI and EcoRI, they were inserted at the same sites of vector pGEX-3X (product of Pharmacia Co.). The resultant chimeric plasmids were used to transform *E. coli* JM109 by a common method, and the desired *E. coli* clones were obtained.

The *E. coli* clones were shake cultured in LB medium until the OD₅₅₀ approached 0.3, and then IPTG was added to a final concentration of 1 mM, and shake culturing was continued for another 1-3 hours to induce expression of the desired proteins.

One-step affinity chromatography, and when necessary also ion exchange and gel filtration chromatography, were used to purify the expressed proteins from the fractions obtained by disrupting the cells with enzymes and ultrasonic treatment.

Binding of carrier protein and desired peptide

This was accomplished using KLH (keyhole limpet hemocyanin) as the carrier protein. That is, 100 µl of 15 mg/ml MBS (m-maleimidobenzoyl-N-hydroxysuccinimide ester) (dimethylformamide solution) was added to 10 mg/ml KLH (0.01 M phosphate buffer, pH 7.0) from which the low molecular impurities had been removed by dialysis, and the mixture was gently stirred at room temperature for 30 minutes to activate the KLH.

After removing the unreacted substance from the activated KLH using a PD-10 column (product of Pharmacia Co.), the desired peptide fragments (5 mg/ml of the synthetic peptides (1)-(4)) dissolved beforehand in a 6 M guanidine-HCl/0.01 M phosphate buffer (pH 7.0) were added, the pH was adjusted to 7.3, and after stirring at room temperature for 3 hours, the unreacted substances were removed by dialysis to prepare immunogen.

Example 5: Antibody production

A 2 ml portion of the immunogen (1 mg/ml) obtained in Example 4 was mixed with an equivalent of Freund's complete adjuvant and emulsified, and then used to immunize Japanese white house rabbits (body weight: 2 kg) at 4 locations under the dorsal skin. After 2 weeks, the same amount of immunogen was mixed with an equivalent of Freund's incomplete adjuvant and emulsified, and used for booster immunization which was continued 2-3 times at 2-3 week intervals. At one week after the final immunization, blood was taken by a normal method and antiserum was obtained. The specific antibody titer of the obtained antiserum was measured based on the ELISA method described below.

For measurement of the serum antibody titer by the ELISA method, each the aforementioned synthetic peptides (1) to (4) was diluted in a carbonate buffer (pH 9.6) to 30 µg/ml and dispensed into a 96-well multiplate (product of Sumitomo Bakelite Co.) at 100 µl/well and left overnight at 4°C for adsorption. After washing with a PBST buffer (phosphate buffer (pH 7.4) containing 0.05% Tween20), 1% bovine serum albumin was added at 100 µl/well for blocking, after which washing was performed with the same type of PBST buffer and 100 to 10,000-fold diluted solutions of the antiserum were added at 100 µl/well and reacted at room temperature for 2 hours.

After washing with PBST, a 1000-fold diluted solution of alkaline phosphate-labelled anti-rabbit serum (goat) was added at 100 µl/well and reacted at room temperature for 2 hours. After the reaction, washing was performed with the same type of PBST buffer and then a solution of the substrate sodium p-nitrophenylphosphate dissolved at 1 mg/ml in a diethanolamine buffer (pH 9.8) was added at 100 µl/well for coloration at room temperature, and this was followed by colorimetry at 405 nm.

The results confirmed an increase in the specific antibodies against the synthetic peptides of interest.

Example 6: Inhibition of *Porphyromonas* bacteria adhesion by antibodies

The adhesion inhibition test for *P. gingivalis* was carried out based on the following method. Five milligrams of hydroxyapatite (HA) granules of size 100-150 µm were placed in a 96-well multiplate, sterilized bland saliva was added and allowed to act at room temperature for 2 hours, and when the saliva components had been adsorbed onto the HA surface it was then washed with a KCl buffer (pH 6.0) and used as the adsorbed hydroxyapatite (S-HA).

P. gingivalis ATCC33277 (10⁷ cells) labelled with ³H-thymidine were added to the above-mentioned S-HA and reacted at room temperature for one hour for adhesion onto the S-HA. After completion of the reaction, washing was performed with the same type of buffer, and the cells adhering to the S-HA were counted with a liquid scintillation counter to determine the degree of adhesion of *P. gingivalis*.

The adhesion-inhibiting effects on the peptides of interest were determined by adding the test antibodies (antibodies against peptides (1) to (4)) to the experimental system described above, and the adhesion inhibition rates are shown in Table 2 as percentages with respect to the control.

Table 2

Adhesion-inhibiting effect of antibodies on <i>P. gingivalis</i>	
Peptide antigen	Adhesion inhibition rate (%)
(1)	72.1
(2)	33.6
(3)	53.6
(4)	89.9

The results shown in Table 2 indicate that the antibodies against peptides (1) to (4) significantly inhibit adhesion of *Porphyromonas gingivalis* to S-HA, thus confirming the usefulness of these antibodies.

Example 7: Formula for periodontal disease prophylactic

(1) Dentifrice	
dibasic calcium phosphate • 2H ₂ O	50.0%
sorbit	10.0%
glycerin	10.0%
carrageenan	1.0%
sodium lauryl sulfate	1.0%
aromatics	1.0%
saccharin	0.1%
ethanol	2.0%
triclosan	0.05%
anti-fimbria fragment goat milk antibody	0.2%
water	remainder
	100.0%

(2) Dentifrice	
silicic anhydride	30.0%
glycerin	30.0%
sorbit	20.0%
carboxymethyl cellulose	1.0%
sodium lauryl sulfate	1.2%
aromatics	1.0%
saccharin	0.1%
ethanol	2.0%
tranexamic acid	0.05%
anti-fimbria fragment cow milk antibody	0.1%
water	remainder
	100.0%

(3) Dentifrice	
aluminum hydroxide	45.0%
sorbit	20.0%
carrageenan	0.5%
carboxymethyl cellulose	1.0%
lauryl diethanolamide	1.0%
sucrose monolaurate	2.0%
aromatics	1.0%
saccharin	0.1%
anti-fimbria fragment sheep serum antibody	0.2%
water	remainder
	100.0%

(4) Dentifrice	
dibasic calcium phosphate • 2H ₂ O	45.0%
carboxymethyl cellulose	1.0%
carrageenan	0.5%
sorbit	35.0%
propylene glycol	3.0%
N-lauroylmethyltaurine sodium	0.5%
gelatin	1.0%
ethyl peroxybenzoate	0.2%
saccharin sodium	0.1%
aromatics	1.1%
magnesium ascorbate phosphate ester	0.5%
anti-fimbria fragment hen egg antibody	0.5%
water	remainder
	100.0%

(5) Dentifrice	
Aluminum hydroxide	40.0%
carboxymethyl cellulose	1.0%
carrageenan	0.5%
sorbit	30.0%
propylene glycol	3.0%
N-myristylmethyltaurine sodium	0.5%
peptide	1.0%
methyl peroxybenzoate	0.2%
saccharin sodium	0.1%
aromatics	1.1%
cetyl pyridinium chloride	0.5%
anti-fimbria fragment horse serum antibody	0.5%
water	remainder
	100.0%

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(6) Mouthwash	
ethanol	20.0%
aromatics	1.0%
saccharin	0.05%
lauryl diethanolamide	0.3%
chlorhexidine gluconate	0.01%
anti-fimbria fragment cow milk antibody	0.1%
water	remainder
	100.0%

(7) Mouthwash	
sorbit	10.0%
ethanol	20.0%
N-palmitoylmethyltaurine sodium	0.5%
POE (20) sorbitan monooleate	1.0%
collagen	0.5%
methyl peroxybenzoate	0.1%
saccharin sodium	0.1%
aromatics	0.5%
anti-fimbria fragment hen egg antibody	0.4%
water	remainder
	100.0%

(8) Tablets	
gum Arabic	6.0%
glucose	72.0%
gelatin	3.0%
aromatics	0.2%
1-menthol	0.1%
spearmint oil	0.1%
sodium ascorbate	0.1%
anti-fimbria fragment sheep milk antibody	0.1%
water	remainder
	100.0%

(9) Gum	
gum base	43.9%
calcium carbonate	2.0%
starch syrup	15.0%
sugar	30.0%
sucrose palmitate	1.0%
fructose	4.0%
aldose	3.0%
aromatics	1.0%
anti-fimbria fragment hen egg antibody	0.1%
	100.0%

(10) Ice cream	
cream (50% nonfat)	16.84%
sugar-free nonfat condensed milk	24.24%
sugar	11.25%
corn syrup	4.65%
stabilizers	0.35%
anti-fimbria fragment antibody-containing cow milk	37.67%
anti-fimbria fragment antibody-containing egg yolk	5.00%
	100.0%

INDUSTRIAL APPLICABILITY

When sequence portions of nucleic acids coding for fimbriin proteins of *Porphyromonas gingivalis* cloned according to the present invention which are specific to the individual strains are used as probes, those individual strains may be separately detected, and when portions with high homology among the individual strains are used as probes, one or a few such probes may be used to detect microorganisms of the species *Porphyromonas gingivalis*. Likewise, individual strains may be separately detected by using antibodies against portions of the amino acid sequences of the fimbriin proteins which are specific to the individual strains, and microorganisms of *Porphyromonas gingivalis* bacteria may be detected by using one or a few different antibodies against amino acid sequences with high homology among the different strains; furthermore, one or a few different antibodies may be used to inhibit adhesion of *Porphyromonas gingivalis* bacteria to teeth.

SEQUENCE LISTING

SEQ ID NO: 1

Sequence Length: 1309

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: 381

Feature

DNA containing fim A gene

216 - 218 Start codon

1257 - 1259 Stop codon

Sequence:

```

AGCACAAAT AATCTGAACG AACTGCCGACG CTATATGCAA GACAATCTCT AAATGGGAAA 60
AGATTAGATT TTTAGAAAAC AATATTCCTT TTTAAAACAA AAACGAGATG AAAAAAACAA 120
AGTTTTTCTT GTTGGGACTT GCTGCTCTTG CTATGACAGC TTGTAACAAA GACAACGAGG 180
CAGAACCCGT TACAGAAGGT AATGCCACCA TCAGCGTGGT ATTGAAGACC AGCAATTCGA 240
ATCGTGCTTT TGGAGTTGGC GATGACGAAT CAAAGGTGGC TAAGTTGACC GTAATGTTTT 300
ATAATGGAGA ACAGCAGGAA GCCATCAAAT CAGCCGAAAA TCGCGACTAAG GTTGAAGACA 360
TCAAATGTAG TGCAGGCCAA CGTACGCTGG TCGTAATGGC CAATACGGGT GCAATGGAAC 420
TGGTTGGCAA GACTCTTGCA GAGGTAAAAG CATTGACAAC TGAAGTACT GCAGAAAACC 480
AAGAGGCTGC AGGGTTGATC ATGACAGCAG AGCCAAAAAC AATCGTTTTG AAGGCAGGCA 540
AGAACTACAT TGGATACAGT GGAACCGGAG AGGGTAATCA CATTGAGAAT GATCCTCTTA 600
AGATCAAGCG TGTTCATGCT CGCATGGCTT TCACCGAAAT TAAAGTGCAA ATGAGCGCAG 660
CCTACGATAA CATTTACACA TTCGTCCCTG AAAAGATTTA TGGTCTCATT GCAAAGAAGC 720
AATCTAATTT GTTCGGGGCA ACACTCGTAA ATGCAGACGC TAATTATCTG ACAGGTTCTT 780
TGACCACATT TAACGGTGCT TACACACCTG CCAACTATGC CAATGTGCCT TGGCTGAGCC 840
GTAATTACGT TGCACCTGCC GCCGATGCTC CTCAGGGTTT CTACGTATTA GAAAATGACT 900
ACTCAGTAA CGGTGGAAC ATTATCCGA CAATCCTGTG TGTTTATGGC AAACCTCAGA 960
AAAACGGAGC CGACTTGCGG GGAGCCGATT TAGCAGCTGC TCAGGCCGCC AATTGGGTGG 1020
ATGCAGAAGG CAAGACCTAT TACCCTGTAT TGGTAACTT CAACAGCAAC AACTATACTT 1080
ATGACAGCAA TTATACGCCT AAGAATAAAA TTGAGCGTAA CCATAAGTAT GATATTAAGT 1140
TGACAATTAC AGGCCCCGGA ACGAATAACC CAGAGAATCC TATCACAGAG TCTGCTCACT 1200
TGAATGTACA GTGCACTGTA GCTGAGTGGG TTCTCGTTGG TCAGAATGCT ACTTGGTAAT 1260
CGACCCGTCA AACGACTAAA AAACCTTTCAT AGTTTGTCTA TATCGGAAT 1309

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SEQ ID NO: 2

Sequence Length: 1309

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: ATCC33227

Feature

DNA containing fim A gene

216 - 218 Start codon

1257 - 1259 Stop codon

Sequence:

```

AGCACAAAT AATCTGAACG AACTGCGACG CTATATGCAA GACAATCTCT AAATGGGAAA 60
AGATTAGATT TTTAGAAAAC AATATTCACT TTAAAAACAA AAACGAGATG AAAAAACAA 120
AGTTTTCTTT GTTGGGACTT GCTGCTCTTG CTATGACAGC TTGTAACAAA GACAACGAGG 180
CAGAACCCGT TACAGAAGGT AATGCCACCA TCAGCGTGGT ATTGAAGACC AGCAATTCGA 240
ATCGTGCTTT TGGAGTTGGC GATGACGAAT CAAAGGTGGC TAAGTTGACC GTAATGGTTT 300
ATAATGGAGA ACAGCAGGAA GCCATCAAAT CAGCCGAAAA TGCGACTAAG GTTGAAGACA 360
TCAAATGTAG TGCAGGCCAA CGTACGCTGG TCGTAATGGC CAATACGGGT GCAATGGAAC 420
TGTTTGCAA GACTCTTGCA GAGGTAAAAG CATTGACAAC TGAAGTACT GCAGAAAACC 480
AAGAGCTGC AGGGTTGATC ATGACAGCAG AGCCAAAAAC AATCGTTTTG AAGGCAGGCA 540
AGAACTACAT TGGATACAGT GGAACCGGAG AGGGTAATCA CATTGAGAAT GATCCTCTTA 600
AGATCAAGCG TGTTTCATGCT CGCATGGCTT TCACCGAAAT TAAAGTGCAA ATGAGCGCAG 660
CCTACGATAA CATTTACACA TTCGTCCCTG AAAAGATTTA TGGTCTCATT GCAAAGAAGC 720
AATCTAATTT GTTCGGGGCA AACTCGTAA ATGCAGACGC TAATTATCTG ACAGGTTCTT 780
TGACCACATT TAACGGTGCT TACACACCTG CCAACTATGC CAATGTGCCT TGGCTGAGCC 840
GTAATTACGT TGCACCTGCC GCCGATGCTC CTCAGGGTTT CTACGTATTA GAAAATGACT 900
ACTCAGCTAA CGGTGGAAC ATTATCCGA CAATCCTGTG TGTTTATGGC AAACCTCAGA 960
AAAACGGAGC CGACTTGGCG GGAGCCGATT TAGCAGCTGC TCAGGCCGCC AATTGGGTGG 1020
ATGCAGAAGG CAAGACCTAT TACCCTGTAT TGGTAACTT CAACAGCAAC AACTATACTT 1080
ATGACAGCAA TTATACGCTT AAGAATAAAA TTGAGCGTAA CCATAAGTAT GATATTAAGT 1140
TGACAATTAC AGGCCCCGGA ACGAATAACC CAGAGAATCC TATCACAGAG TCTGCTCACT 1200
TGAATGTACA GTGCACTGTA GCTGAGTGGG TTCTCGTTGG TCAGAATGCT ACTTGGAAT 1260
CGACCCGTCA AACGACTAAA AAACCTTCAT AGTTTGCTA TATCGGAAT 1309

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SEQ ID NO: 3

Sequence Length: 1309

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: BH18/10

Feature

DNA containing fim A gene

216 - 218 Start codon

1257 - 1259 Stop codon

Sequence:

```

AGCACAAACAT AATCTGAACG AACTGCGACG CTATATGCAA GACAATCTCT AAATGGGAAA 60
AGATTAGATT TTTAGAAAAC AATATTCACT TTTAAAAACA AAACGAGATG AAAAAACAA 120
AGTTTTTCTT GTTGGGACTT GCTGCTCTTG CTATGACAGC TTGTAACAAA GACAACGAGG 180
CAGAACCCGT TACAGAAGGT AATGCCACCA TCAGCGTGGT ATTGAAGACC AGCAATTCTGA 240
ATCGTGCTTT TGGAGTTGGC GATGACGAAT CAAAGGTGGC TAAGTTGACC GTAATGGTTT 300
ATAATGGAGA ACAGCAGGAA GCCATCAAAT CAGCCGAAAA TCGGACTAAG GTTGAAGACA 360
TCAAATGTAG TGCAGGCCAA CGTACGCTGG TCGTAATGGC CAATACGGGT GCAATGGAAC 420
TGGTTGGCAA GACTCTTGCA GAGGTAAAG CATTGACAAC TGAATGACT GCAGAAAACC 480
AAGAGGCTGC AGGTTTGATC ATGACAGCAG AGCCAAAAAC AATCGTTTTG AAGGCAGGCA 540
AGAACTACAT TGGATACAGT GGAACCGGAG AGGGTAATCA CATTGAGAAT GATCCTCTTA 600
AGATCAAGCG TGTTTCATGCT CGCATGGCTT TCACCGAAAT TAAAGTGCAA ATGAGCGCAG 660
CCTACGATAA CATTTACACA TTCGTCCCTG AAAAGATTTA TGGTCTCATT GCAAAGAAGC 720
AATCTAATTT GTTCGGGGCA ACACTCGTAA ATGCAGACGC TAATTATCTG ACAGGTTCTT 780
TGACCACATT TAACGGTGCT TACACACCTG CCAACTATGC CAATGTGCCT TGGCTGAGCC 840
GTAATTGCGT TGCACCTGCC GCCGATGCTC CTCAGGGTTT CTACGTATTA GAAAATGACT 900
ACTCAGCTAA CGGTGGAAC ATTCTCCGA CAATCCTGTG TGTTTATGGC AAACCTCAGA 960
AAAACGGAGC CGACTTGGCG GGAGCCGATT TAGCAGCTGC TCAGGCCGCC AATTGGGTGG 1020
ATGCAGAAGG CAAGACCTAT TACCCTGTAT TGGTAACTT CAACAGCAAC AACTATACTT 1080
ATGACAGCAA TTATAGCCTT AAGAATAAAA TTGAGCGTAA CCATAAGTAT GATATTAAGT 1140
TGACAATTAC AGGCCCGGA ACGAATAACC CAGAGAATCC TATCACAGAG TCTGCTCACT 1200
TGAATGTACA GTGCACTGTA GCTGAGTGGG TTCTCGTTGG TCAGAATGCT ACTTGTAAT 1260
CGACCCGTCA AACGACTAAA AAACTTTCAT AGTTTGTCTA TATCGGAAT 1309

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SEQ ID NO: 4

Sequence Length: 1306

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: HW24D-1

Feature

DNA containing fim A gene

211 - 213 Start codon

1255 - 1257 Stop codon

Sequence:

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AGCACAAACAC AATCTGAACG AACTACGACG CTATATGCAA GACAATCTCT AAATGGGAAA 60

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AGATTCTTAG AAAACAATAT TCACTTTTAA AACAAAAACG AGATGAAAAA AACAAAGTTT 120
TTCTTGTTGG GACTTGCTGC TCTTGCTATG ACAGCTTGTA ACAAAGACAA CGAGGCAGAA 180
CCC GTTACAG AAGGTAATGC TACCATCAGC GTGGTATTGA AGACCAGCAA TCCGAATCGT 240
GCTTTTGGAG AAGACGAATC AAAGGTGGCT AAGTTGACCG TAATGGTTTA TAATGGAGAA 300
CAGCAGGAAG CCATCAAATC AGCCGAAAAAT GCGACTAAGG TTGAAGACAT CAAATGTAGT 360
GCAGGCCAAC GTACGCTGGT CGTAATGGCC AATACGGGTG AAATGAAATT GGCTGGCAAG 420
ACTCTTGCGAG AGGTAAAAGC ATTGACAACT GAACTGACTG CAGAAAACCA AGAGGCTGCA 480
GGGTTGATCA TGACGGCAGA GCCTGTTGAG GTAACACTTG TCGCCGGCAA TAACTATTAT 540
GGTTATGATG GATCTCAGGG AGGTAATCAG ATTCGCAAG ATACTCCTCT TGAAATCAAA 600
CGTGTTTCATG CTCGCATGGC TTTCACCGAA ATTAAAGTGC AGATGAGTCC GTCTTATGTT 660
AACAAATACA ATTTTGCCCC CGAAAACATC TATGCACTTG TGGCTAAAAA GGAGTCTAAT 720
CTATTCGGTG CTTCAATTGGC AAATAGTGAT GATGCTTATT TGA CTG GTT TTTGACGAAT 780
TTCAACGGTG CTTATTCCCC TGCAAACTAT ACTCATGTTG ACTGGTTGGG AAGAGACTAC 840
ACAGAGCCTT CCAATAATGC TCCACAAGGT TTCTATGTTT TGGAGAGCAC ATACGCTCAG 900
AATGCAGGTC TACGTCTAC TATTCTATGT GTAAAAGGCA AGCTGACAAA GCATGATGGT 960
ACTCCTTTGA GTTCTGAGGA AATGACAGCT GCATTCAATG CCGGCTGGAT TGTTCAGAC 1020
AATAATCCTA CGACCTATTA CCCTGTATTG GTAAACTTCA ACAGCAACAA CTATACTTAT 1080
GACAATGGTT ATACGCCTAA GAATAAAATT GAGCGTAACC ATAAGTATGA TATTAAGTTG 1140
ACAATTACAG GCCCCGGAAC GAATAACCCA GAGAATCCTA TCACAGAGTC TGCTCACTTG 1200
AATGTACAGT GCACTGTAGC TGAGTGGGTT CTCGTTGGTC AGAATGCTAC TTGGTAATCG 1260
ACCCTCAAAC GACTAAAAAA CTTTCATAGT TTGTCTATAT CGGAAT 1306

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SEQ ID NO: 5

Sequence Length: 1306

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: OMZ314

Feature

DNA containing fim A gene

211 - 213 Start codon

1252 - 1254 Stop codon

Sequence:

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AGCACACAT AATCTGAACG AACTACGACG CTATATGCAA GACAATCTCT AAATGGGAAA 60
AGATTCTTAG AAAACAATAT TCACTTTTAA AACAAAAACG AGATGAAAAA AACAAAGTTT 120
TTCTTGTTGG GACTTGCTGC TCTTGCTATG ACAGCTTGTA ACAAAGACAA CGAGGCAGAA 180
CCC GTTACAG AAGGTAATGC TACCATCAGC GTGGTATTGA AGACCAGCAA TCCGAATCGT 240
GCTTTTGGAG AAGACGAATC AAAGGTGGCT AAGTTGACCG TAATGGTTTA TAATGGAGAA 300
CAGCAGGAAG CCATCAAATC AGCCGAAAAAT GCGACTAAGG TTGAAGACAT CAAATGTAGT 360
GCAGGCCAAC GTACGCTGGT CGTAATGGCC AATACGGGTG AAATGAAATT GGCTGGCAAG 420

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ACTCTTGCAG AGGTAAAAGC ATTGACAACCT GAACTGACTG CAGAAAACCA AGAGGCTGCA 480
 GGGTTGATCA TGACAGCAGA GCCTGTTGAG GTAACACTTG TCGCCGGCAA TAACTATTAT 540
 5 GGTATGATG GATCTCAGGG AGGTAATCAG ATTTGCAAG ATACTCCTCT TGAAATCAAA 600
 CGTGTTTCATG CTCGCATGGC TTTCACCGAA ATTAAAGTGC AGATGAGTCC GTCTTATGTT 660
 AACAAATACA ATTTTGCCCC CGAAAACATC TATGCACTTG TGGCTAAAAA GGAGTCTAAT 720
 CTATTCGGTG CTTTATTGGC AAATAGTGAT GATGCTTATT TGACTGGTTC TTTGACGAAT 780
 10 TTCAACGGTG CTTATTCCCC TGCAAACTAT ACTCATGTTG ACTGTTGGG AAGAGACTAC 840
 ACAGAGCCTT CCAATAATGC TCCACAAGGT TTCTATGTTT TGGAGAGCAC ATACGCTCAG 900
 AATGCAGGTC TACGTCCTAC TATTCTATGT GTAAAAGGCA AGCTGACAAA GCATGATGGT 960
 ACTCCTTTGA GTTCTGAGGA AATGACAGCT GCATTCAATG CCGGCTGGAT TGTTCAGAC 1020
 AATAATCCTA CGACCTATTA CCCTGTATTG GTAACTTCA ACAGCAACAA CTATACTTAT 1080
 15 GACAATGGTT ATACGCCTAA GAATAAAATT GAGCGTAACC ATAAGTATGA TATTAAGTTG 1140
 ACAATTACAG GCCCCGGAAC GAATAACCCA GAGAATCCTA TCACAGAGTC TGCTCACTTG 1200
 AATGTACAGT GCACTGTAGC TGAGTGGGTT CTCGTTGGTC AGAATGCTAC TTGATAATCG 1260
 GCCCTCAAAC GACTAAAAAA CTTTCATAGT TTGTCTATAT CGGAAT 1306

SEQ ID NO: 6

Sequence Length: 1311

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: OMZ409

Feature

DNA containing fim A gene

216 - 218 Start codon

1260 - 1262 Stop codon

Sequence:

AGCACAAACAT AATCTGAACG AACTACGACG CTATATGCAA GACAATCTCT AAATGGGAAA 60
 AGATTAGATT CTTAGAAAAC AATATTCACCT TTAAAAACAA AAACGAGATG AAAAAAACAA 120
 40 AGTTTTTCTT GTTGGGACTT GCTGCTCTTG CTATGACAGC TTGTAACAAA GACAACGAGG 180
 CAGAACCCGT TACAGAAGGT AATGCTACCA TCAGCGTGGT TTTGAAGACC AGCAATCCGA 240
 ATCGTGCTTT TGGAGAAGAC GAATCAAAGG TGGCTAAGTT GACCGTAATG GTTTATAATG 300
 GAGAACAGCA GGAAGCCATC AAATCAGCCG AAAATGCGAC TAAGGTTGAA GACATCAAAT 360
 45 GTAGTGACAG CCAACGTACG CTGGTCGTAA TGGCCAATAC GGGTGCAATG GAACTGGTTG 420
 GCAAGACTCT TGCAGAGGTA AAAGCATTGA CAACTGAACT GACTGCAGAA AACCAAGAGG 480
 CTACAGGTTT GATCATGACA GCAGAGCCTG TTGACGTAAC ACTTGTGCGC GGCAATAACT 540
 ATTATGGTTA TGATGGATCT CAGGGAGGTA ATCAGATTTC GCAGGATACT CCTCTTGAAA 600
 50 TCAAACGTGT TCATGCTCGC ATGGCTTTCA CCGAAATTAA AGTGCAGATG AGTCCGTCTT 660
 ATGTTAACAA ATACAATTTT GCCCCGAAA ACATCTATGC ACTTGTGGCT AAAAAGGAGT 720
 CTAATCTATT CGGTGCTTCA TTGGCAAATA GTGATGATGC TTATTTGACT GGTTCCTTGA 780

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CGAATTTCAA CGGTGCTTAT TCCCCTGCAA ACTATACTCA TGTTGACTGG TTGGGAAGAG 840
 ACTACACAGA GCCTTCCAAT AATGCTCCAC AAGGTTTCTA TGTTTTGGAG AGCACATACG 900
 CTCAGAATGC AGGTCTACGT CCTACTATTC TATGTGTAAA AGGCAAGCTG ACAAAGCATG 960
 ATGGTACTCC TTTGAGTTCT GAGGAAATGA CAGCTGCATT CAATGCCGGC TGGATTGTTG 1020
 CAGACAATAA TCCTACGACC TATTACCCCTG TATTGGTAAA CTTCAACAGC AACAACTATA 1080
 CTTATGACAA TGGTTATACG CCTAAGAATA AAATTGAGCG TAACCATAAG TATGATATTA 1140
 AGTTGACAAT TACAGGCCCC GGAACGAATA ACCCAGAGAA TCCTATCACA GAGTCTGCTC 1200
 ACTTGAATGT ACAGTGCACG GTAGCTGAGT GGGTTCTCGT TGGTCAGAAT GCTACTTGGT 1260
 AATCGACCCT CAAACGACTA AAAAATTTC ATAGTTTGTC TATATCGGAA T 1311

SEQ ID NO: 7

Sequence Length: 1318

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: ATCC49417

Feature

DNA containing fim A gene

216 - 218 Start codon

1266 - 1268 Stop codon

Sequence:

AGCACAAAC AATCTGAACG AACTACGACG CTATATGCAA GACAATCTCT AAATGGGAAA 60
 AGATTAGATT CTTAGAAAAC AATATTCACG TTTAAAAACA AAACGAGATG AAAAAAACAA 120
 AGTTTTTCTT GTTGGGACTT GCTGCTCTTG CTATGACAGC TTGTAACAAA GACAACGAGG 180
 CAGAACCCTG TACAGAAGGT AATGCTACCA TCAGCGTGGT ATTGAAGACC AGCAATCCGA 240
 ATCGTGCTTT TGGAAATGCG GGAGACGAAG CAAAAGTGGC TAAGTTGACC GTAATGGTTT 300
 ACAAGGGTGA ACAGCAGGAA GCCATCAAA CAGCCGAAAA TGCGACTAAG GTTGAAAACA 360
 TCAATGTAG TGCAGGCCAA CGTACGCTGG TCGTAATGGC CAATACGGGT GGAATGGAAT 420
 TGGCTGGCAA GACTCTTGCA GAGGTAAAAG CATTGACAAC TGAAGTACT GAAGGAAACC 480
 AAGAGGCTGC AGGGTTGATC ATGACAGCAG AGCCTGTTGA GGTAACACTT GTCGCCGGCA 540
 ATAACATTA TGGTTATGAT GGATCTCAGG GAGGTAATCA GATTTGCAA GATACTCTC 600
 TTGAAATCAA ACGTGTTCTG GCCCGTATTG CGTTCACCAA GATTGAAGTG ACGATGAGCC 660
 AGTCTTATGC GAACAAATAC AATTTTGCCC CCGAAAACAT CTATGCACTT GTGGCTAAAA 720
 AGAAGTCTAA TCTATTCCGT GCTTCATTGG CAAATAATGA TGATGCTTAT TTGACTGGTT 780
 CTTTGACGAC TTTCAACGGA GCTTATACCC CTGCAAACTA TACTCATGTC GACTGGTTGG 840
 GAAGAGACTT CACAGAGCCT TCCAATAATG CTCCACAAGG TTTCTATGTT TTGGAGAGCA 900
 CATACGCTCA GAATGCAGGT CTACGTCCTA CTATTCTATG TATAAAAGGC AAGCTGACAA 960
 AGCATGATGG TACTCCTTTG AGTCTGAGG AAATGACAGC TGCATTCAAT GCCGGCTGGA 1020
 TTGTTGCAAA CAATGATCCT ACGACCTATT ATCCTGTATT AGTGAACCTT GAGAGCAATA 1080
 ATTACACCTA CACAGGTGAG GCTGTTGAGA AAGGAAAAAT CGTTCGTAAC CATAAATTCG 1140

ACATCAACCT GACGATCACC GGTCTGGTA CGAATAATCC TGAAAACCCC ATTACTGAGT 1200
CTGCTAACCT CAACGTTAAT TGTGTGGTTG CTGCCTGGAA AGGTGTTGTA CAAAATGTTA 1260
TTTGTAATC GACCCGTCAA ACGACTAAAA AACTTTCATA GTTTGTCTAT ATCGGAAT 1318
SEQ ID NO: 8

Sequence Length: 1314

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: 6/26

Feature

DNA containing fim A gene

211 - 213 Start codon

1270 - 1272 Stop codon

Sequence:

AGCACAACAT AATCTGAACG AACTGCGACG CTATATGCAA GACAATCTCT AAATGGAAAA 60
AGATTCTTAG AAAACAATAT TCACTTTTAA AACAAAAACG AGATGAAAAA AACAAAGTTT 120
TTCTTGTTGG GACTTGCTGC TCTTGCTATG ACAGCTTGTA ACAAAGACAA CGAGGCAGAA 180
CCCGTTACAG AAAGTAATGC TACCATCAGC GTGGTATTGA AGACCAGCAA TCCGAATCGT 240
GCTTTTGGAA ATGCGGGAGA CGAAGCAAAA GTGGCTAAAC TGACTGTAAT GGTTTACAAG 300
GGTGAGCAGC AGGAAGCCAT CAAATCAGTC GAAAATGCAA TTAAGGTTGA AAACATCAAA 360
TGTGGTGCAG GCCAACGTAC GCTGGTTGTA ATGGCCAATA CGGGTGAAT GGAATTGGCT 420
GGCAAACTC TTGCAGAGGT AAAAGCATTG ACAACTGAAC TGACTGAAGG AAACCAAGAG 480
GCTGCAGGGT TGATCATGAC AGCAGAGCCT GTTGAGGTAA CACTTGTCGC CGGCAATAAC 540
TATTATGGTT ATGATGGATC TCAGGGAGGT AATCAGATTT CGCAAGGTAC TCCTCTTGAA 600
ATCAAACGTG TTCATGCCCG TATTGCGTTC ACCAAGATTG AAGTGACGAT GAGCCAGTCT 660
TATGCGAACA AATACAATTT TGCCCCGAA AACATCTATG CACTTGTCGC TAAAAAGAAG 720
TCTAATCTAT TCGGTGCTTC ATTGGCAAAT AGTGATGATG CTTATTTGAC TGGTTCTTTG 780
ACGACTTTCA ACGGTGCTTA TTCCCCTGCA AACTATACTC ATGTTGACTG GTTGGGAAGA 840
GACTACACAG AAATAGGAGC CGCTACTGTT AATACTCCGA AGGGATTCTA TGTCTTGGAG 900
AGCACATACG CTCAGAATGC AGGTCTACGT CCTACTATTC TATGTGTAAG AGGCAAGCTG 960
ACAAAGCATG ATGGTACAGC TTTGAGTTCT GAGGAAATGA CAGCTGCATT CAATGCCGGC 1020
TGGATTGTTG CAAACAATGA TCCTACGACC TATTATCCTG TATTAGTGAA CTTTGAGAGC 1080
AATAATTACA CCTACACAGG TGAGCGTGTT GAGAAAGGAA AAATCGTTTC TAACCATAAG 1140
TTCGACATCA ACCTGACGAT CACCGGTCCT GGCACGAATA ATCCTGAAAA CCCCATTACT 1200
GAGTCTGCTA ACCTCAACGT TAATTGTGTG GTTGCTGCAT GGAAAGGTGT TGTACAAAAT 1260
GTTATTTGGT AATCAGCTCA TCAAAAACT TTCATAGTTT GTCTATATCG GAAT 1314

SEQ ID NO: 9

Sequence Length: 1319

Sequence Type: Nucleic acid

Strandedness: Double strand

Molecular Type: genomic DNA

Original Source

Organism: Porphyromonas gingivalis

Strain: HG564

Feature

DNA containing fim A gene

187 - 189 Start codon

1267 - 1269 Stop codon

Sequence:

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AGCACAAACAC AATCTGAACG AACTGCGACG CTATATGCAA GACAATCTCT AAATGGAAAA 60
AGATTCTTAG AAAACAATAT TCACTTTTAA AACAAAAACG AGATGAAAAA AACAAAGTTT 120
TTCTTGTTGG GACTTGCTGC TCTTGCTATG ACAGCTTGTA ACAAAGACAA CGAGGCAGAA 180
CCCATTGTGG AAAGTGAACG TACTGTTAGT TTCATAATTA AGAGCGGAGA GGGCGGTGCT 240
GTAGGCGATG GCCTTGACAG TGCCAAGATC ACAAAGTCA CCGCCATGGT CTATGCAGGT 300
CAAATTCAAG AAGGGATTAA GACAGTGGAA GAGGCCGACG GAGTTCTTAA AGTAGAAGGA 360
ATTCCGTGTA AATCAGGAGC CAACCGTGTC CTCGTCGTTG TAGCTAATCA CAATTATGAG 420
CTTACCGGTA AAAGTTTGAA TGAGGTTGAG GCCTTGACGA CTTCTTTGAC AGCTGAAAAC 480
CAAAATGCCA AAAACTTGAT CATGACAGGT AAGTCAGCAG CTTTACAAT CAAGCCGGGC 540
TCCAACCACT ATGGCTATCC TGATGGGACT ACATCCGACA ACCTTGTTTC TGCTGGAAC 600
CCTCTTGCCG TTAATCGCGT GCATGCCGGT ATCTCATTCC CAGGAGTAGA GGTAATATG 660
GCTACACAGT ATCAAACTA CTACTCTTTT AACCAGCTG ACGCTAAAAT CGCAGCCCTT 720
GTCGCAAGA AAGATTCTAA GATTTTCGGC AATTCTTTGG TCTCAAACAC TAATGCATAT 780
TTGTATGGAG TCCAACGCC TGCCGGTCTT TACACTCCGG ATGCTGCAGG AGAAACATAC 840
GAATTGGAGG CGTCTTTGAA TACGAATTAT GCTGTAGGTG CCGGCTTCTA TGTGCTGGAA 900
AGTAAATATG ATGCAAGCAA CGAGCTTCGT CCGACGATCC TTTGTATCTA TGGAAAGCTG 960
CTCGATAAGG ACGGCAACCC TCTCACGGAA CCAGCCTTGA CGGATGCTAT AAATGCCGGA 1020
TTCTGCGACG GAGATGGCAC GACTTACTAT CCGGTATTGG TGAAGTATGA TGGCAATGGC 1080
TACATCTATT CAGGTGCTAT TACCAAGGA CAAAACAAAA TCGTTCGCAA CAACCACTAC 1140
AAGATTACGC TGAACATCAC CGGCCCGGT ACGAATACTC CTGAAAATCC TCAACCGGTA 1200
CAAGCCAACC TGAATGTTAC TTGCCAAGTT ACACCTGGG TTGTTGTTAA TCAGGCTGCT 1260
ACTTGGTAAT CGACCCGTCA AACGACTAAA AAACCTTTCAT AGTTTGTCTA TATCGGAAT 1319

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SEQ ID NO: 10

Sequence Length: 347

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Protein

Feature: Amino acid sequence of finbrillin of
Porphyromonas gingivalis 381

Sequence:

EP 0 726 314 A1

Met Val Leu Lys Thr Ser Asn Ser Asn Arg Ala Phe Gly Val Gly Asp
-10 -5 -1 1 5
5 Asp Glu Ser Lys Val Ala Lys Leu Thr Val Met Val Tyr Asn Gly Glu
10 10 15 20
Gln Gln Glu Ala Ile Lys Ser Ala Glu Asn Ala Thr Lys Val Glu Asp
25 30 35
10 Ile Lys Cys Ser Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr
40 45 50
Gly Ala Met Glu Leu Val Gly Lys Thr Leu Ala Glu Val Lys Ala Leu
55 60 65 70
15 Thr Thr Glu Leu Thr Ala Glu Asn Gln Glu Ala Ala Gly Leu Ile Met
75 80 85
Thr Ala Glu Pro Lys Thr Ile Val Leu Lys Ala Gly Lys Asn Tyr Ile
90 95 100
20 Gly Tyr Ser Gly Thr Gly Glu Gly Asn His Ile Glu Asn Asp Pro Leu
105 110 115
Lys Ile Lys Arg Val His Ala Arg Met Ala Phe Thr Glu Ile Lys Val
120 125 130
Gln Met Ser Ala Ala Tyr Asp Asn Ile Tyr Thr Phe Val Pro Glu Lys
135 140 145 150
25 Ile Tyr Gly Leu Ile Ala Lys Lys Gln Ser Asn Leu Phe Gly Ala Thr
155 160 165
Leu Val Asn Ala Asp Ala Asn Tyr Leu Thr Gly Ser Leu Thr Thr Phe
170 175 180
30 Asn Gly Ala Tyr Thr Pro Ala Asn Tyr Ala Asn Val Pro Trp Leu Ser
185 190 195
Arg Asn Tyr Val Ala Pro Ala Ala Asp Ala Pro Gln Gly Phe Tyr Val
200 205 210
35 Leu Glu Asn Asp Tyr Ser Ala Asn Gly Gly Thr Ile His Pro Thr Ile
215 220 225 230
Leu Cys Val Tyr Gly Lys Leu Gln Lys Asn Gly Ala Asp Leu Ala Gly
235 240 245
40 Ala Asp Leu Ala Ala Ala Gln Ala Ala Asn Trp Val Asp Ala Glu Gly
250 255 260
Lys Thr Tyr Tyr Pro Val Leu Val Asn Phe Asn Ser Asn Asn Tyr Thr
265 270 275
45 Tyr Asp Ser Asn Tyr Thr Pro Lys Asn Lys Ile Glu Arg Asn His Lys
280 285 290
Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly Thr Asn Asn Pro Glu
295 300 305 310
Asn Pro Ile Thr Glu Ser Ala His Leu Asn Val Gln Cys Thr Val Ala
315 320 325
50 Glu Trp Val Leu Val Gly Gln Asn Ala Thr Trp
330 335

55

SEQ ID NO: 11

Sequence Length: 347

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Protein

Feature: Amino acid sequence of finbrillin of
Porphyromonas gingivalis ATCC33277

Sequence:

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Met Val Leu Lys Thr Ser Asn Ser Asn Arg Ala Phe Gly Val Gly Asp
-10          -5          -1  1          5
Asp Glu Ser Lys Val Ala Lys Leu Thr Val Met Val Tyr Asn Gly Glu
      10          15          20
Gln Gln Glu Ala Ile Lys Ser Ala Glu Asn Ala Thr Lys Val Glu Asp
      25          30          35
Ile Lys Cys Ser Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr
      40          45          50
Gly Ala Met Glu Leu Val Gly Lys Thr Leu Ala Glu Val Lys Ala Leu
      55          60          65          70
Thr Thr Glu Leu Thr Ala Glu Asn Gln Glu Ala Ala Gly Leu Ile Met
      75          80          85
Thr Ala Glu Pro Lys Thr Ile Val Leu Lys Ala Gly Lys Asn Tyr Ile
      90          95          100
Gly Tyr Ser Gly Thr Gly Glu Gly Asn His Ile Glu Asn Asp Pro Leu
      105          110          115
Lys Ile Lys Arg Val His Ala Arg Met Ala Phe Thr Glu Ile Lys Val
      120          125          130
Gln Met Ser Ala Ala Tyr Asp Asn Ile Tyr Thr Phe Val Pro Glu Lys
      135          140          145          150
Ile Tyr Gly Leu Ile Ala Lys Lys Gln Ser Asn Leu Phe Gly Ala Thr
      155          160          165
Leu Val Asn Ala Asp Ala Asn Tyr Leu Thr Gly Ser Leu Thr Thr Phe
      170          175          180
Asn Gly Ala Tyr Thr Pro Ala Asn Tyr Ala Asn Val Pro Trp Leu Ser
      185          190          195
Arg Asn Tyr Val Ala Pro Ala Ala Asp Ala Pro Gln Gly Phe Tyr Val
      200          205          210
Leu Glu Asn Asp Tyr Ser Ala Asn Gly Gly Thr Ile His Pro Thr Ile
      215          220          225          230
Leu Cys Val Tyr Gly Lys Leu Gln Lys Asn Gly Ala Asp Leu Ala Gly
      235          240          245
Ala Asp Leu Ala Ala Ala Gln Ala Ala Asn Trp Val Asp Ala Glu Gly
      250          255          260

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Lys Thr Tyr Tyr Pro Val Leu Val Asn Phe Asn Ser Asn Asn Tyr Thr
 265 270 275
 Tyr Asp Ser Asn Tyr Thr Pro Lys Asn Lys Ile Glu Arg Asn His Lys
 280 285 290
 Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly Thr Asn Asn Pro Glu
 295 300 305 310
 Asn Pro Ile Thr Glu Ser Ala His Leu Asn Val Gln Cys Thr Val Ala
 315 320 325
 Glu Trp Val Leu Val Gly Gln Asn Ala Thr Trp
 330 335

SEQ ID NO: 12

Sequence Length: 347

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Protein

Feature: Amino acid sequence of finbrillin of
 Porphyromonas gingivalis BH18/10

Sequence:

Met Val Leu Lys Thr Ser Asn Ser Asn Arg Ala Phe Gly Val Gly Asp
 -10 -5 -1 1 5
 Asp Glu Ser Lys Val Ala Lys Leu Thr Val Met Val Tyr Asn Gly Glu
 10 15 20
 Gln Gln Glu Ala Ile Lys Ser Ala Glu Asn Ala Thr Lys Val Glu Asp
 25 30 35
 Ile Lys Cys Ser Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr
 40 45 50
 Gly Ala Met Glu Leu Val Gly Lys Thr Leu Ala Glu Val Lys Ala Leu
 55 60 65 70
 Thr Thr Glu Leu Thr Ala Glu Asn Gln Glu Ala Ala Gly Leu Ile Met
 75 80 85
 Thr Ala Glu Pro Lys Thr Ile Val Leu Lys Ala Gly Lys Asn Tyr Ile
 90 95 100
 Gly Tyr Ser Gly Thr Gly Glu Gly Asn His Ile Glu Asn Asp Pro Leu
 105 110 115
 Lys Ile Lys Arg Val His Ala Arg Met Ala Phe Thr Glu Ile Lys Val
 120 125 130
 Gln Met Ser Ala Ala Tyr Asp Asn Ile Tyr Thr Phe Val Pro Glu Lys
 135 140 145 150
 Ile Tyr Gly Leu Ile Ala Lys Lys Gln Ser Asn Leu Phe Gly Ala Thr
 155 160 165
 Leu Val Asn Ala Asp Ala Asn Tyr Leu Thr Gly Ser Leu Thr Thr Phe
 170 175 180

EP 0 726 314 A1

Asn Gly Ala Tyr Thr Pro Ala Asn Tyr Ala Asn Val Pro Trp Leu Ser
 185 190 195
 Arg Asn Cys Val Ala Pro Ala Ala Asp Ala Pro Gln Gly Phe Tyr Val
 200 205 210
 Leu Glu Asn Asp Tyr Ser Ala Asn Gly Gly Thr Ile His Pro Thr Ile
 215 220 225 230
 Leu Cys Val Tyr Gly Lys Leu Gln Lys Asn Gly Ala Asp Leu Ala Gly
 235 240 245
 Ala Asp Leu Ala Ala Ala Gln Ala Ala Asn Trp Val Asp Ala Glu Gly
 250 255 260
 Lys Thr Tyr Tyr Pro Val Leu Val Asn Phe Asn Ser Asn Asn Tyr Thr
 265 270 275
 Tyr Asp Ser Asn Tyr Thr Pro Lys Asn Lys Ile Glu Arg Asn His Lys
 280 285 290
 Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly Thr Asn Asn Pro Glu
 295 300 305 310
 Asn Pro Ile Thr Glu Ser Ala His Leu Asn Val Gln Cys Thr Val Ala
 315 320 325
 Glu Trp Val Leu Val Gly Gln Asn Ala Thr Trp
 330 335
 SEQ ID NO: 13
 Sequence Length: 348
 Sequence Type: Amino acid
 Topology: Linear
 Molecular Type: Protein
 Feature: Amino acid sequence of finbrillin of
 Porphyromonas gingivalis HW24D1
 Sequence:
 Met Val Leu Lys Thr Ser Asn Pro Asn Arg Ala Phe Gly Glu Asp Glu
 -10 -5 -1 1 5
 Ser Lys Val Ala Lys Leu Thr Val Met Val Tyr Asn Gly Glu Gln Gln
 10 15 20
 Glu Ala Ile Lys Ser Ala Glu Asn Ala Thr Lys Val Glu Asp Ile Lys
 25 30 35
 Cys Ser Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr Gly Glu
 40 45 50
 Met Lys Leu Ala Gly Lys Thr Leu Ala Glu Val Lys Ala Leu Thr Thr
 55 60 65 70
 Glu Leu Thr Ala Glu Asn Gln Glu Ala Ala Gly Leu Ile Met Thr Ala
 75 80 85
 Glu Pro Val Glu Val Thr Leu Val Ala Gly Asn Asn Tyr Tyr Gly Tyr
 90 95 100

EP 0 726 314 A1

Asp Gly Ser Gln Gly Gly Asn Gln Ile Ser Gln Asp Thr Pro Leu Glu
 105 110 115
 Ile Lys Arg Val His Ala Arg Met Ala Phe Thr Glu Ile Lys Val Gln
 120 125 130
 Met Ser Pro Ser Tyr Val Asn Lys Tyr Asn Phe Ala Pro Glu Asn Ile
 135 140 145 150
 Tyr Ala Leu Val Ala Lys Lys Glu Ser Asn Leu Phe Gly Ala Ser Leu
 155 160 165
 Ala Asn Ser Asp Asp Ala Tyr Leu Thr Gly Ser Leu Thr Asn Phe Asn
 170 175 180
 Gly Ala Tyr Ser Pro Ala Asn Tyr Thr His Val Asp Trp Leu Gly Arg
 185 190 195
 Asp Tyr Thr Glu Pro Ser Asn Asn Ala Pro Gln Gly Phe Tyr Val Leu
 200 205 210
 Glu Ser Thr Tyr Ala Gln Asn Ala Gly Leu Arg Pro Thr Ile Leu Cys
 215 220 225 230
 Val Lys Gly Lys Leu Thr Lys His Asp Gly Thr Pro Leu Ser Ser Glu
 235 240 245
 Glu Met Thr Ala Ala Phe Asn Ala Gly Trp Ile Val Ala Asp Asn Asn
 250 255 260
 Pro Thr Thr Tyr Tyr Pro Val Leu Val Asn Phe Asn Ser Asn Asn Tyr
 265 270 275
 Thr Tyr Asp Asn Gly Tyr Thr Pro Lys Asn Lys Ile Glu Arg Asn His
 280 285 290
 Lys Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly Thr Asn Asn Pro
 295 300 305 310
 Glu Asn Pro Ile Thr Glu Ser Ala His Leu Asn Val Gln Cys Thr Val
 315 320 325
 Ala Glu Trp Val Leu Val Gly Gln Asn Ala Thr Trp
 330 335

SEQ ID NO: 14

Sequence Length: 347

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Protein

Feature: Amino acid sequence of finbrillin of
 Porphyromonas gingivalis OMZ314

Sequence:

Met Val Leu Lys Thr Ser Asn Pro Asn Arg Ala Phe Gly Glu Asp Glu
 -10 -5 -1 1 5
 Ser Lys Val Ala Lys Leu Thr Val Met Val Tyr Asn Gly Glu Gln Gln
 10 15 20

EP 0 726 314 A1

Glu Ala Ile Lys Ser Ala Glu Asn Ala Thr Lys Val Glu Asp Ile Lys
 25 30 35
 5 Cys Ser Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr Gly Glu
 40 45 50
 Met Lys Leu Ala Gly Lys Thr Leu Ala Glu Val Lys Ala Leu Thr Thr
 55 60 65 70
 10 Glu Leu Thr Ala Glu Asn Gln Glu Ala Ala Gly Leu Ile Met Thr Ala
 75 80 85
 Glu Pro Val Glu Val Thr Leu Val Ala Gly Asn Asn Tyr Tyr Gly Tyr
 90 95 100
 15 Asp Gly Ser Gln Gly Gly Asn Gln Ile Ser Gln Asp Thr Pro Leu Glu
 105 110 115
 Ile Lys Arg Val His Ala Arg Met Ala Phe Thr Glu Ile Lys Val Gln
 120 125 130
 20 Met Ser Pro Ser Tyr Val Asn Lys Tyr Asn Phe Ala Pro Glu Asn Ile
 135 140 145 150
 Tyr Ala Leu Val Ala Lys Lys Glu Ser Asn Leu Phe Gly Ala Ser Leu
 155 160 165
 25 Ala Asn Ser Asp Asp Ala Tyr Leu Thr Gly Ser Leu Thr Asn Phe Asn
 170 175 180
 Gly Ala Tyr Ser Pro Ala Asn Tyr Thr His Val Asp Trp Leu Gly Arg
 185 190 195
 Asp Tyr Thr Glu Pro Ser Asn Asn Ala Pro Gln Gly Phe Tyr Val Leu
 200 205 210
 30 Glu Ser Thr Tyr Ala Gln Asn Ala Gly Leu Arg Pro Thr Ile Leu Cys
 215 220 225 230
 Val Lys Gly Lys Leu Thr Lys His Asp Gly Thr Pro Leu Ser Ser Glu
 235 240 245
 35 Glu Met Thr Ala Ala Phe Asn Ala Gly Trp Ile Val Ala Asp Asn Asn
 250 255 260
 Pro Thr Thr Tyr Tyr Pro Val Leu Val Asn Phe Asn Ser Asn Asn Tyr
 265 270 275
 40 Thr Tyr Asp Asn Gly Tyr Thr Pro Lys Asn Lys Ile Glu Arg Asn His
 280 285 290
 Lys Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly Thr Asn Asn Pro
 295 300 305 310
 45 Glu Asn Pro Ile Thr Glu Ser Ala His Leu Asn Val Gln Cys Thr Val
 315 320 325
 Ala Glu Trp Val Leu Val Gly Gln Asn Ala Thr
 330 335
 50 SEQ ID NO: 15
 Sequence Length: 348
 Sequence Type: Amino acid
 55

Topology: Linear

Molecular Type: Protein

Feature: Amino acid sequence of finbrillin of
Porphyromonas gingivalis OMZ409

Sequence:

Met Val Leu Lys Thr Ser Asn Pro Asn Arg Ala Phe Gly Glu Asp Glu
-10 -5 -1 1 5

Ser Lys Val Ala Lys Leu Thr Val Met Val Tyr Asn Gly Glu Gln Gln
10 15 20

Glu Ala Ile Lys Ser Ala Glu Asn Ala Thr Lys Val Glu Asp Ile Lys
25 30 35

Cys Ser Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr Gly Ala
40 45 50

Met Glu Leu Val Gly Lys Thr Leu Ala Glu Val Lys Ala Leu Thr Thr
55 60 65 70

Glu Leu Thr Ala Glu Asn Gln Glu Ala Thr Gly Leu Ile Met Thr Ala
75 80 85

Glu Pro Val Asp Val Thr Leu Val Ala Gly Asn Asn Tyr Tyr Gly Tyr
90 95 100

Asp Gly Ser Gln Gly Gly Asn Gln Ile Ser Gln Asp Thr Pro Leu Glu
105 110 115

Ile Lys Arg Val His Ala Arg Met Ala Phe Thr Glu Ile Lys Val Gln
120 125 130

Met Ser Pro Ser Tyr Val Asn Lys Tyr Asn Phe Ala Pro Glu Asn Ile
135 140 145 150

Tyr Ala Leu Val Ala Lys Lys Glu Ser Asn Leu Phe Gly Ala Ser Leu
155 160 165

Ala Asn Ser Asp Asp Ala Tyr Leu Thr Gly Ser Leu Thr Asn Phe Asn
170 175 180

Gly Ala Tyr Ser Pro Ala Asn Tyr Thr His Val Asp Trp Leu Gly Arg
185 190 195

Asp Tyr Thr Glu Pro Ser Asn Asn Ala Pro Gln Gly Phe Tyr Val Leu
200 205 210

Glu Ser Thr Tyr Ala Gln Asn Ala Gly Leu Arg Pro Thr Ile Leu Cys
215 220 225 230

Val Lys Gly Lys Leu Thr Lys His Asp Gly Thr Pro Leu Ser Ser Glu
235 240 245

Glu Met Thr Ala Ala Phe Asn Ala Gly Trp Ile Val Ala Asp Asn Asn
250 255 260

Pro Thr Thr Tyr Tyr Pro Val Leu Val Asn Phe Asn Ser Asn Asn Tyr
265 270 275

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Thr Tyr Asp Asn Gly Tyr Thr Pro Lys Asn Lys Ile Glu Arg Asn His
 280 285 290
 Lys Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly Thr Asn Asn Pro
 295 300 305 310
 Glu Asn Pro Ile Thr Glu Ser Ala His Leu Asn Val Gln Cys Thr Val
 315 320 325
 Ala Glu Trp Val Leu Val Gly Gln Asn Ala Thr Trp
 330 335
 SEQ ID NO: 16
 Sequence Length: 350
 Sequence Type: Amino acid
 Topology: Linear
 Molecular Type: Protein
 Feature: Amino acid sequence of finbrillin of
 Porphyromonas gingivalis ATCC49417
 Sequence:
 Met Val Leu Lys Thr Ser Asn Pro Asn Arg Ala Phe Gly Asn Ala Gly
 -10 -5 -1 1 5
 Asp Glu Ala Lys Val Ala Lys Leu Thr Val Met Val Tyr Lys Gly Glu
 10 15 20
 Gln Gln Glu Ala Ile Lys Ser Ala Glu Asn Ala Thr Lys Val Glu Asn
 25 30 35
 Ile Lys Cys Ser Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr
 40 45 50
 Gly Gly Met Glu Leu Ala Gly Lys Thr Leu Ala Glu Val Lys Ala Leu
 55 60 65 70
 Thr Thr Glu Leu Thr Glu Gly Asn Gln Glu Ala Ala Gly Leu Ile Met
 75 80 85
 Thr Ala Glu Pro Val Glu Val Thr Leu Val Ala Gly Asn Asn Tyr Tyr
 90 95 100
 Gly Tyr Asp Gly Ser Gln Gly Gly Asn Gln Ile Ser Gln Asp Thr Pro
 105 110 115
 Leu Glu Ile Lys Arg Val Arg Ala Arg Ile Ala Phe Thr Lys Ile Glu
 120 125 130
 Val Thr Met Ser Gln Ser Tyr Ala Asn Lys Tyr Asn Phe Ala Pro Glu
 135 140 145 150
 Asn Ile Tyr Ala Leu Val Ala Lys Lys Lys Ser Asn Leu Phe Gly Ala
 155 160 165
 Ser Leu Ala Asn Asn Asp Asp Ala Tyr Leu Thr Gly Ser Leu Thr Thr
 170 175 180
 Phe Asn Gly Ala Tyr Thr Pro Ala Asn Tyr Thr His Val Asp Trp Leu
 185 190 195

EP 0 726 314 A1

Gly Arg Asp Phe Thr Glu Pro Ser Asn Asn Ala Pro Gln Gly Phe Tyr
 200 205 210
 Val Leu Glu Ser Thr Tyr Ala Gln Asn Ala Gly Leu Arg Pro Thr Ile
 215 220 225 230
 Leu Cys Ile Lys Gly Lys Leu Thr Lys His Asp Gly Thr Pro Leu Ser
 235 240 245
 Ser Glu Glu Met Thr Ala Ala Phe Asn Ala Gly Trp Ile Val Ala Asn
 250 255 260
 Asn Asp Pro Thr Thr Tyr Tyr Pro Val Leu Val Asn Phe Glu Ser Asn
 265 270 275
 Asn Tyr Thr Tyr Thr Gly Glu Ala Val Glu Lys Gly Lys Ile Val Arg
 280 285 290
 Asn His Lys Phe Asp Ile Asn Leu Thr Ile Thr Gly Pro Gly Thr Asn
 295 300 305 310
 Asn Pro Glu Asn Pro Ile Thr Glu Ser Ala Asn Leu Asn Val Asn Cys
 315 320 325
 Val Val Ala Ala Trp Lys Gly Val Val Gln Asn Val Ile Trp
 330 335 340

SEQ ID NO: 17

Sequence Length: 353

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Protein

Feature: Amino acid sequence of finbrillin of
 Porphyromonas gingivalis 6/26

Sequence:

Met Val Leu Lys Thr Ser Asn Pro Asn Arg Ala Phe Gly Asn Ala Gly
 -10 -5 -1 1 5
 Asp Glu Ala Lys Val Ala Lys Leu Thr Val Met Val Tyr Lys Gly Glu
 10 15 20
 Gln Gln Glu Ala Ile Lys Ser Val Glu Asn Ala Ile Lys Val Glu Asn
 25 30 35
 Ile Lys Cys Gly Ala Gly Gln Arg Thr Leu Val Val Met Ala Asn Thr
 40 45 50
 Gly Gly Met Glu Leu Ala Gly Lys Thr Leu Ala Glu Val Lys Ala Leu
 55 60 65 70
 Thr Thr Glu Leu Thr Glu Gly Asn Gln Glu Ala Ala Gly Leu Ile Met
 75 80 85
 Thr Ala Glu Pro Val Glu Val Thr Leu Val Ala Gly Asn Asn Tyr Tyr
 90 95 100
 Gly Tyr Asp Gly Ser Gln Gly Gly Asn Gln Ile Ser Gln Gly Thr Pro
 105 110 115

EP 0 726 314 A1

5 Leu Glu Ile Lys Arg Val His Ala Arg Ile Ala Phe Thr Lys Ile Glu
 120 125 130
 Val Thr Met Ser Gln Ser Tyr Ala Asn Lys Tyr Asn Phe Ala Pro Glu
 135 140 145 150
 Asn Ile Tyr Ala Leu Val Ala Lys Lys Lys Ser Asn Leu Phe Gly Ala
 155 160 165
 10 Ser Leu Ala Asn Ser Asp Asp Ala Tyr Leu Thr Gly Ser Leu Thr Thr
 170 175 180
 Phe Asn Gly Ala Tyr Ser Pro Ala Asn Tyr Thr His Val Asp Trp Leu
 185 190 195
 Gly Arg Asp Tyr Thr Glu Ile Gly Ala Ala Thr Val Asn Thr Pro Lys
 200 205 210
 15 Gly Phe Tyr Val Leu Glu Ser Thr Tyr Ala Gln Asn Ala Gly Leu Arg
 215 220 225 230
 Pro Thr Ile Leu Cys Val Lys Gly Lys Leu Thr Lys His Asp Gly Thr
 235 240 245
 20 Ala Leu Ser Ser Glu Glu Met Thr Ala Ala Phe Asn Ala Gly Trp Ile
 250 255 260
 Val Ala Asn Asn Asp Pro Thr Thr Tyr Tyr Pro Val Leu Val Asn Phe
 265 270 275
 25 Glu Ser Asn Asn Tyr Thr Tyr Thr Gly Glu Ala Val Glu Lys Gly Lys
 280 285 290
 Ile Val Arg Asn His Lys Phe Asp Ile Asn Leu Thr Ile Thr Gly Pro
 295 300 305 310
 30 Gly Thr Asn Asn Pro Glu Asn Pro Ile Thr Glu Ser Ala Asn Leu Asn
 315 320 325
 Val Asn Cys Val Val Ala Ala Trp Lys Gly Val Val Gln Asn Val Ile
 330 335 340

Trp

SEQ ID NO: 18

Sequence Length: 360

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Protein

Feature: Amino acid sequence of finbrillin of
 Porphyromonas gingivalis HG564

Sequence:

Met Glu Thr Asp Ala Thr Val Ser Phe Ile Ile Lys Ser Gly Glu Gly
 -15 -10 -5
 50 Arg Ala Val Gly Asp Gly Leu Ala Asp Ala Lys Ile Thr Lys Leu Thr
 -1 1 5 10 15

EP 0 726 314 A1

Ala Met Val Tyr Ala Gly Gln Ile Gln Glu Gly Ile Lys Thr Val Glu
20 25 30
5 Glu Ala Asp Gly Val Leu Lys Val Glu Gly Ile Pro Cys Lys Ser Gly
35 40 45
Ala Asn Arg Val Leu Val Val Val Ala Asn His Asn Tyr Glu Leu Thr
50 55 60
10 Gly Lys Ser Leu Asn Glu Val Glu Ala Leu Thr Thr Ser Leu Thr Ala
65 70 75
Glu Asn Gln Asn Ala Lys Asn Leu Ile Met Thr Gly Lys Ser Ala Ala
80 85 90 95
15 Phe Thr Ile Lys Pro Gly Ser Asn His Tyr Gly Tyr Pro Asp Gly Thr
100 105 110
Thr Ser Asp Asn Leu Val Ser Ala Gly Thr Pro Leu Ala Val Thr Arg
115 120 125
20 Val His Ala Gly Ile Ser Phe Ala Gly Val Glu Val Asn Met Ala Thr
130 135 140
Gln Tyr Gln Asn Tyr Tyr Ser Phe Asn Pro Ala Asp Ala Lys Ile Ala
145 150 155
25 Ala Leu Val Ala Lys Lys Asp Ser Lys Ile Phe Gly Asn Ser Leu Val
160 165 170 175
Ser Asn Thr Asn Ala Tyr Leu Tyr Gly Val Gln Thr Pro Ala Gly Leu
180 185 190
Tyr Thr Pro Asp Ala Ala Gly Glu Thr Tyr Glu Leu Glu Ala Ser Leu
195 200 205
30 Asn Thr Asn Tyr Ala Val Gly Ala Gly Phe Tyr Val Leu Glu Ser Lys
210 215 220
Tyr Asp Ala Ser Asn Glu Leu Arg Pro Thr Ile Leu Cys Ile Tyr Gly
225 230 235
35 Lys Leu Leu Asp Lys Asp Gly Asn Pro Leu Thr Glu Pro Ala Leu Thr
240 245 250 255
Asp Ala Ile Asn Ala Gly Phe Cys Asp Gly Asp Gly Thr Thr Tyr Tyr
260 265 270
40 Pro Val Leu Val Asn Tyr Asp Gly Asn Gly Tyr Ile Tyr Ser Gly Ala
275 280 285
Ile Thr Gln Gly Gln Asn Lys Ile Val Arg Asn Asn His Tyr Lys Ile
290 295 300
45 Thr Leu Asn Ile Thr Gly Pro Gly Thr Asn Thr Pro Glu Asn Pro Gln
305 310 315
Pro Val Gln Ala Asn Leu Asn Val Thr Cys Gln Val Thr Pro Trp Val
320 325 330 335
50 Val Val Asn Gln Ala Ala Thr Trp
340

SEQ ID NO: 19

Sequence Length: 30

Sequence Type: Nucleic acid

Topology: Linear

Molecular Type: Synthetic DNA

Sequence:

AATTGGATCC GCGCAGCAAG GCCAGCCCGG

30

SEQ ID NO: 20

Sequence Length: 30

Sequence Type: Nucleic acid

Topology: Linear

Molecular Type: Synthetic DNA

Sequence:

AGAGGGATCC GAGCGAACCC CGCTCCCTGT

30

SEQ ID NO: 21

Sequence Length: 23

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Hypothetical

Feature:

X₀₁=Asn or Lys; X₀₂=Ala or Val; X₀₃=Thr or

Ile; X₀₄=Asp or Asn; X₀₅=Ser or Gly

Sequence:

X₀₁ Gly Glu Gln Gln Glu Ala Ile Lys Ser X₀₂ Glu Asn Ala X₀₃ Lys

5

10

15

Val Glu X₀₄ Ile Lys Cys X₀₅

20

SEQ ID NO: 22

Sequence Length: 29

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Hypothetical

Feature:

X₀₁=Asp or Asn; X₀₂=Ser or Gly; X₀₃=Ala, Glu or

Gly; X₀₄=Glu or Lys; X₀₅=Val or Ala

Sequence:

Glu X₀₁ Ile Lys Cys X₀₂ Ala Gly Gln Arg Thr Leu Val Val Met Ala

5

10

15

Asn Thr Gly X_m Met X_n Leu X_n Gly Lys Thr Leu Ala
 20 25

SEQ ID NO: 23

Sequence Length: 31

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Hypothetical

Feature:

X₀₁=Val or Ala; X₀₂=Ala or Glu; X₀₃=Glu or Gly

Sequence:

X₀₁ Gly Lys Thr Leu Ala Glu Val Lys Ala Leu Thr Thr Glu Leu Thr
 5 10 15
 X₀₂ X₀₃ Asn Gln Glu Ala Ala Gly Leu Ile Met Thr Ala Glu Pro
 20 25 30

SEQ ID NO: 24

Sequence Length: 13

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Hypothetical

Feature:

X₀₁=Asn or Ser; X₀₂=Thr, Asp or Lys; X₀₃=Ala,

Ser or Asp; X₀₄=Gln or Ala; X₀₅=Asn or Ser

Sequence:

Gln Gly Phe Tyr Val Leu Glu X₀₁ X₀₂ Tyr X₀₃ X₀₄ X₀₅
 5 10

SEQ ID NO: 25

Sequence Length: 18

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Hypothetical

Feature:

X₀₁=Gly or Pro; X₀₂=Thr or Lys; X₀₃=Phe or

Tyr; X₀₄=Asn, Glu or Asp; X₀₅=Ser or Gly; X₀₆=

Asn or Gly; X₀₇=Thr or Ile

Sequence:

X₀₁ X₀₂ Thr Tyr Tyr Pro Val Leu Val Asn X₀₃ X₀₄ X₀₅ Asn X₀₆ Tyr
 5 10 15
 X₀₇ Tyr

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SEQ ID NO: 26

Sequence Length: 34

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Hypothetical

Feature:

X_{01} =Ser or Asn; X_{02} =Asn or Gly

Sequence:

Ser Asn Asn Tyr Thr Tyr Asp X₀₁ X₀₂ Tyr Thr Pro Lys Asn Lys Ile

5 10 15
Glu Arg Asn His Lys Tyr Asp Ile Lys Leu Thr Ile Thr Gly Pro Gly
20 25 30

Thr Asn

SEQ ID NO: 27

Sequence Length: 37

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Hypothetical

Feature:

X_{01} =Asn or Thr; X_{02} =Ile or Gln; X_{03} =His or Asn

Sequence :

Ile Thr Gly Pro Gly Thr Asn X₆₁ Pro Glu Asn Pro X₆₂ Thr Glu Ser

Ala X₀₀ Leu Asn Val Gln Cys Thr Val Ala Glu Trp Val Leu Val Gly

Gln Asn Ala Thr Trp
35

SEQ ID NO: 28

Sequence Length: 17

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Hypothetical

Feature:

X_{01} =Thr or Asn; X_{02} =Ser or Thr; X_{03} =Thr or Ala

Sequence:

Thr Gly Ser Leu Thr X₀₁ Phe Asn Gly Ala Tyr X₀₂ Pro Ala Asn Tyr
5 10 15

 X_{03}

SEQ ID NO: 29

Sequence Length: 18

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Synthetic Peptide

Sequence:

Glu Leu Thr Ala Glu Asn Gln Glu Ala Ala Gly Leu Ile Met Thr Ala
5 10 15

Glu Pro

SEQ ID NO: 30

Sequence Length: 14

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Synthetic Peptide

Sequence:

Gly Ser Leu Thr Thr Phe Asn Gly Ala Tyr Ser Pro Ala Asn
5 10

SEQ ID NO: 31

Sequence Length: 15

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Synthetic Peptide

Sequence:

Thr Tyr Tyr Pro Val Leu Val Asn Phe Asn Ser Asn Asn Tyr Thr
5 10 15

SEQ ID NO: 32

Sequence Length: 17

Sequence Type: Amino acid

Topology: Linear

Molecular Type: Synthetic Peptide

Sequence:

Pro Gly Thr Asn Asn Pro Glu Asn Pro Ile Thr Glu Ser Ala His Leu
5 10 15

Asn

Claims

1. DNA coding for the fimbrillin protein of *Porphyromonas gingivalis* strains ATCC33277, BH18/10, HW24D-1, OMZ314, OMZ409, ATCC49417, 6/26 or HG564, which is included in the base sequences represented by any of Sequence Nos. 2 through 9.

2. DNA having any base sequence forming a region comprising at least 10 contiguous bases, with at least 50% base sequence homology between at least 2 different base sequences of the base sequences listed as Sequence Nos. 1 through 9.
- 5 3. DNA according to claim 2, wherein said homology is at least 70%.
4. DNA according to claim 3, wherein said homology is at least 90%.
- 10 5. DNA according to claim 4, wherein the length of the homologous region consisting of said contiguous bases is at least 30 bases.
6. DNA having any base sequence forming a region comprising at least 10 contiguous bases, with less than 50% base sequence homology between at least 2 different base sequences of the base sequences listed as Sequence Nos. 1 through 9.
- 15 7. DNA according to claim 6, wherein said homology is 30% or less.
8. A fimbriin protein of *Porphyromonas gingivalis* having an amino acid sequence represented by any of Sequence Nos. 11 through 18.
- 20 9. A peptide having any amino acid sequence forming a region comprising at least 5 contiguous amino acids, with at least 50% amino acid sequence homology between at least 2 different amino acid sequences of the amino acid sequences listed as Sequence Nos. 10 through 18.
- 25 10. A peptide according to claim 9, wherein said homology is at least 70%.
11. A peptide according to claim 10, wherein said homology is at least 90%.
- 30 12. A peptide having any amino acid sequence forming a region comprising at least 5 continuously linked amino acids, with less than 50% amino acid sequence homology between at least 2 different amino acid sequences of the amino acid sequences listed as Sequence Nos. 10 through 18.
13. A peptide according to claim 12, wherein said homology is 40% or less.
- 35 14. An expression vector comprising DNA according to any of claims 1 to 7.
15. A host possessing an expression vector according to claim 14.
- 40 16. A peptide consisting of at least 5 contiguous amino acids of any of the amino acid sequences listed as Sequence Nos. 21 through 28.
17. A peptide having any of the amino acid sequences listed as Sequence Nos. 29 through 32.
- 45 18. A complex formed by binding a carrier protein with a peptide according to any of claims 9 through 13.
19. A complex formed by binding a carrier protein with a peptide according to claim 16.
20. A composite antigen formed by binding a carrier protein with a peptide according to claim 17.
- 50 21. An antibody against a peptide or protein according to any of claims 8 to 13 or 16 to 19.
22. An agent for the prevention or improvement of periodontal diseases which contains an antibody according to claim 21.

55

Fig.1

(1)

381	GC	GC	AG	CA	AG	GC	CC	CG	GA	GC	ACA	ACA	TAA	TCT	GA	AC	GA	ACT	GC	GAC	G
ATCC33277	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
BH18/10	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
HW24D1	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
OMZ314	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
OMZ409	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
ATCC49417	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
6/26	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
HG564	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:

(2)

381	CT	AT	AT	GC	AA	GA	CA	AT	CT	CT	AA	AT	GG	GA	AA	AG	AT	TA	GAT	TT	TT	TA	GAA	AA	C
ATCC33277	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
BH18/10	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
HW24D1	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
OMZ314	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
OMZ409	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
ATCC49417	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
6/26	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
HG564	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:

(3)

381	AA	TAT	TCA	CT	TT	TAA	AA	CA	AA	AA	AC	GAG	AT	GA	AA	AA	AA	CA	AA	GT	TT	TT	TCT	T
ATCC33277	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
BH18/10	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
HW24D1	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
OMZ314	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
OMZ409	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
ATCC49417	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
6/26	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
HG564	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:

(4)

381	GT	TGG	GAC	TT	GCT	GCT	CT	TG	CT	AT	GAC	AG	CT	TG	TA	CA	AA	AG	ACA	AC	GAG	G
ATCC33277	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
BH18/10	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
HW24D1	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
OMZ314	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
OMZ409	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
ATCC49417	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
6/26	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:
HG564	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:	:

Fig.2

(5)

```

381      CAGAACCCGTTACAGAAGGTAATGCCACCATCAGCGTGGTATTGAAGACC
ATCC33277  ::::::::::CG::ACA::GG:A:T::C::CA:C::CGTGG:AT:G::::C:
BH18/10    ::::::::::CG::ACA::GG:A:T::C::CA:C::CGTGG:AT:G::::C:
HW24D1     ::::::::::CG::ACA::GG:A:T::T::CA:C::CGTGG:AT:G::::C:
OMZ314     ::::::::::CG::ACA::GG:A:T::T::CA:C::CGTGG:AT:G::::C:
OMZ409     ::::::::::CG::ACA::GG:A:T::T::CA:C::CGTGG:TT:G::::C:
ATCC49417  ::::::::::TG::ACA::GG:A:T::T::CA:C::CGTGG:AT:G::::C:
6/26      ::::::::::CG::ACA::AG:A:T::T::CA:C::CGTGG:AT:G::::C:
HG564     ::::::::::CA::GTG::AC:G:C::T::TG:T::TTTCA:AA:T::::G:

```

(6)

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381      AGCAATTCGAATCGTGCTTTTGGAGTTGGCGATGACGAATCAAAGGTGGC
ATCC33277  A:CA:TTC:AAT:::::T:T::AGTTGGCGAT:ACG:AT:A::GG:GG:
BH18/10    A:CA:TTC:AAT:::::T:T::AGTTGGCGAT:ACG:AT:A::GG:GG:
HW24D1     A:CA:TCC:AAT:::::T:T::AG-----AA:ACG:AT:A::GG:GG:
OMZ314     A:CA:TCC:AAT:::::T:T::AG-----AA:ACG:AT:A::GG:GG:
OMZ409     A:CA:TCC:AAT:::::T:T::AG-----AA:ACG:AT:A::GG:GG:
ATCC49417  A:CA:TCC:AAT:::::T:T::AAATGCGGGA:ACG:AG:A::AG:GG:
6/26      A:CA:TCC:AAT:::::T:T::AAATGCGGGA:ACG:AG:A::AG:GG:
HG564     G:AG:---:GGG:::::G:A::CGATGGCCTT:CAG:TG:C::GA:CA:

```

(7)

```

381      TAAGTTGACCGTAATGGTTTATAATGGAGAACAGCAGGAAGCCATCAAAT
ATCC33277  T::GT:G::C:TA:::::T::TAAT::AG:ACAG::G::::CC::C::AT
BH18/10    T::GT:G::C:TA:::::T::TAAT::AG:ACAG::G::::CC::C::AT
HW24D1     T::GT:G::C:TA:::::T::TAAT::AG:ACAG::G::::CC::C::AT
OMZ314     T::GT:G::C:TA:::::T::TAAT::AG:ACAG::G::::CC::C::AT
OMZ409     T::GT:G::C:TA:::::T::TAAT::AG:ACAG::G::::CC::C::AT
ATCC49417  T::GT:G::C:TA:::::T::CAAG::TG:ACAG::G::::CC::C::AT
6/26      T::AC:G::T:TA:::::T::CAAG::TG:GCAG::G::::CC::C::AT
HG564     A::AC:C::C:CC:::::C::TGCA::TC:AATT::A::::GG::T::GA

```

(8)

```

381      CAGCCGAAAATG-CGAC-----TAAGGTTGAAGACATCAAATGTAGT
ATCC33277  ::::CC:::A:T:-:G:C-----:G::T:::GAC::CAAA:::AGT
BH18/10    ::::CC:::A:T:-:G:C-----:G::T:::GAC::CAAA:::AGT
HW24D1     ::::CC:::A:T:-:G:C-----:G::T:::GAC::CAAA:::AGT
OMZ314     ::::CC:::A:T:-:G:C-----:G::T:::GAC::CAAA:::AGT
OMZ409     ::::CC:::A:T:-:G:C-----:G::T:::GAC::CAAA:::AGT
ATCC49417  ::::CC:::A:T:-:G:C-----:G::T:::AAC::CAAA:::AGT
6/26      ::::TC:::A:T:-:A:T-----:G::T:::AAC::CAAA:::GGT
HG564     ::::TG:::G:G:C:G:CGGAGTTCT:::A::A:::GGA::TCCG:::AAA

```

Fig.3

(9)

381	GCAG--GCCAA-CGTACGCTGGTCGTAATGGCCAAT-ACGGGTGCAATGG
ATCC33277	G:::--:::ACG::G::C::AA::G::C::--::GGG:GCA::GG
BH18/10	G:::--:::ACG::G::C::AA::G::C::--::GGG:GCA::GG
HW24D1	G:::--:::ACG::G::C::AA::G::C::--::GGG:GAA::GA
OMZ314	G:::--:::ACG::G::C::AA::G::C::--::GGG:GAA::GA
OMZ409	G:::--:::ACG::G::C::AA::G::C::--::GGG:GCA::GG
ATCC49417	G:::--:::ACG::G::C::AA::G::C::--::GGG:GGA::GG
6/26	G:::--:::ACG::G::T::AA::G::C::--::GGG:GGA::GG
HG564	T:::GA:::C:::GTC::C::C::TG:A::T:::C::AAT::--:::-G

(10)

381	AACTGGTTGGCAAGACTCTTGCA-GAGGTAAAAGCATTGACAACCTGAACT
ATCC33277	:AC:GGTT::C::G:C:C::C:-:::AA:A::A:::A:::GAAC:
BH18/10	:AC:GGTT::C::G:C:C::C:-:::AA:A::A:::A:::GAAC:
HW24D1	:AT:GGCT::C::G:C:C::C:-:::AA:A::A:::A:::GAAC:
OMZ314	:AT:GGCT::C::G:C:C::C:-:::AA:A::A:::A:::GAAC:
OMZ409	:AC:GGTT::C::G:C:C::C:-:::AA:A::A:::A:::GAAC:
ATCC49417	:AT:GGCT::C::G:C:C::C:-:::AA:A::A:::A:::GAAC:
6/26	:AT:GGCT::C::A:C:C::C:-:::AA:A::A:::A:::GAAC:
HG564	:GC:TACC::T::A:G:-:::A:T:::TG:G::C:::G:::TCTT:

(11)

381	GACTGCAGAAAACCAAGAGGCTGCAGGGTTGATCATGACAGCAGAGCCAA
ATCC33277	:::T:CA:A:::G:G::TGC:GGG:::A:CAG::C:AA
BH18/10	:::T:CA:A:::G:G::TGC:GGG:::A:CAG::C:AA
HW24D1	:::T:CA:A:::G:G::TGC:GGG:::G:CAG::C:TG
OMZ314	:::T:CA:A:::G:G::TGC:GGG:::A:CAG::C:TG
OMZ409	:::T:CA:A:::G:G::TAC:GGT:::A:CAG::C:TG
ATCC49417	:::T:AA:G:::G:G::TGC:GGG:::A:CAG::C:TG
6/26	:::T:AA:G:::G:G::TGC:GGG:::A:CAG::C:TG
HG564	:::A:CT:A:::A:T::CAA:AAC:::A:GTA::T:AG

(12)

381	AAACAATCGTTTGAAGGCAGGCAAGAACTACATTGGATA---CAGTGGA
ATCC33277	AAACAA:CGTTT:GAAGG:A:::AAG:::T:CAT:::A::---CAG:::A
BH18/10	AAACAA:CGTTT:GAAGG:A:::AAG:::T:CAT:::A::---CAG:::A
HW24D1	TTGAGG:AACAC:TGTCG:C:::AAT:::T:TTA:::T::---TGA:::A
OMZ314	TTGAGG:AACAC:TGTCG:C:::AAT:::T:TTA:::T::---TGA:::A
OMZ409	TTGACG:AACAC:TGTCG:C:::AAT:::T:TTA:::T::---TGA:::A
ATCC49417	TTGAGG:AACAC:TGTCG:C:::AAT:::T:TTA:::T::---TGA:::A
6/26	TTGAGG:AACAC:TGTCG:C:::AAT:::T:TTA:::T::---TGA:::A
HG564	CAGCTT:TACAA:CAAGC:G:::TCC:::C:CTA:::C::TCCTGA:::G

Fig.4

(13)

```

381      AC-CGGAGAGGGTAATCACATTGAGAATGA---TCCTCTTAAGATCAAGC
ATCC33277 A:-CGGAGAG:GT::T:ACA::GAGAAT:A---:~::~~::~~::AAGA:C:AG:
BH18/10  A:-CGGAGAG:GT::T:ACA::GAGAAT:A---:~::~~::~~::AAGA:C:AG:
HW24D1   T:TCAGGGA-:GT::T:AGA::TCGCAA:ATAC:~::~~::~~::GAAA:C:AA:
OMZ314   T:TCAGGGA-:GT::T:AGA::TCGCAA:ATAC:~::~~::~~::GAAA:C:AA:
OMZ409   T:TCAGGGA-:GT::T:AGA::TCGCAA:ATAC:~::~~::~~::GAAA:C:AA:
ATCC49417 T:TCAGGGA-:GT::T:AGA::TCGCAA:ATAC:~::~~::~~::GAAA:C:AA:
6/26     T:TCAGGGA-:GT::T:AGA::TCGCAA:ATAC:~::~~::~~::GAAA:C:AA:
HG564    A:T-ACATCC:AC::C:TTG::TCTGCT:GAAC:~::~~::~~::GCCG:T:CT:

```

(14)

```

381      GTGTTTCATGCTCGCATGGCTTTACCGAAATTAAAGTGCAAATGAGCGCA
ATCC33277 :T::T:A::TC:C::GG:T::A:CGAAA:TA:A::GCAA::AGCGCA
BH18/10  :T::T:A::TC:C::GG:T::A:CGAAA:TA:A::GCAA::AGCGCA
HW24D1   :T::T:A::TC:C::GG:T::A:CGAAA:TA:A::GCAG::AGTCCG
OMZ314   :T::T:A::TC:C::GG:T::A:CGAAA:TA:A::GCAG::AGTCCG
OMZ409   :T::T:A::TC:C::GG:T::A:CGAAA:TA:A::GCAG::AGTCCG
ATCC49417 :T::T:A::TC:C::GG:T::A:CGAAA:TA:A::GCAG::AGTCCG
6/26     :T::T:A::TC:C::GG:T::A:CGAAA:TA:A::GCAG::AGTCCG
HG564    :C::G:A::CG:T::CT:A::G:AGGAG:AG:G::AAAT::GCTACA

```

(15)

```

381      GCCTACGATAACATTTACACATTC-GTCC---CTGA---AAAGATTTATGG
ATCC33277 GCC::CGAT::ATT::ACA::C-GT:---:T:---A::G::TTAT:G
BH18/10  GCC::CGAT::ATT::ACA::C-GT:---:T:---A::G::TTAT:G
HW24D1   TCT::TGTT::AAA::AAT::T-GC:---:C:---A::C::CTAT:C
OMZ314   TCT::TGTT::AAA::AAT::T-GC:---:C:---A::C::CTAT:C
OMZ409   TCT::TGTT::AAA::AAT::T-GC:---:C:---A::C::CTAT:C
ATCC49417 TCT::TGCG::AAA::AAT::T-GC:---:C:---A::C::CTAT:C
6/26     TCT::TGCG::AAA::AAT::T-GC:---:C:---A::C::CTAT:C
HG564    CAG::TCAA::TAC::TCT::TAAC:AG:T::CGCT::A::CGCA:C

```

(16)

```

381      TCTCATTGCAAAGAAGCAATCTAATTTGTTTCGGGGCAACACTCGTAAATG
ATCC33277 T::CA:T::A::G::GC:A::~::~~::~~::TT:G::~::~~::~~::GGCAA:AC:C:TAAATG
BH18/10  T::CA:T::A::G::GC:A::~::~~::~~::TT:G::~::~~::~~::GGCAA:AC:C:TAAATG
HW24D1   A::TG:G::T::A::GG:G::~::~~::~~::TC:A::~::~~::~~::TGCTT:AT:G:CAAATA
OMZ314   A::TG:G::T::A::GG:G::~::~~::~~::TC:A::~::~~::~~::TGCTT:AT:G:CAAATA
OMZ409   A::TG:G::T::A::GG:G::~::~~::~~::TC:A::~::~~::~~::TGCTT:AT:G:CAAATA
ATCC49417 A::TG:G::T::A::GA:G::~::~~::~~::TC:A::~::~~::~~::TGCTT:AT:G:CAAATA
6/26     A::TG:G::T::A::GA:G::~::~~::~~::TC:A::~::~~::~~::TGCTT:AT:G:CAAATA
HG564    C::TG:C::A::G::AG:T::~::~~::~~::GA:T::~::~~::~~::CAATT:TT:G:TCTCAA

```

Fig.5

(17)

381	CAGACGCTAATTATCTGACAGGTTCTTTGACCACATTTAACGGTGCTTAC
ATCC33277	CAGACGC:AAT:::C::ACA::TTC:TTG:CC:CATTAA:::TGC:::C
BH18/10	CAGACGC:AAT:::C::ACA::TTC:TTG:CC:CATTAA:::TGC:::C
HW24D1	GTGATGA:GCT:::T::ACT::TTC:TTG:CG:ATTTCAA:::TGC:::T
OMZ314	GTGATGA:GCT:::T::ACT::TTC:TTG:CG:ATTTCAA:::TGC:::T
OMZ409	GTGATGA:GCT:::T::ACT::TTC:TTG:CG:ATTTCAA:::TGC:::T
ATCC49417	ATGATGA:GCT:::T::ACT::TTC:TTG:CG:CTTTCAA:::AGC:::T
6/26	GTGATGA:GCT:::T::ACT::TTC:TTG:CG:CTTTCAA:::TGC:::T
HG564	ACACTAA:GCA:::T::TAT::-AG:CCA:--:CGCCTGC:::TCT:::C

(18)

381	ACACCTGCCAACTATGCCAATGTGCCTTGGCTGAGCCGTAATTACGTTGC
ATCC33277	A:A::T:CCA:CTA:G:CA:T:TGCCTTGGCT:AGCC:TAATTACGTTGC
BH18/10	A:A::T:CCA:CTA:G:CA:T:TGCCTTGGCT:AGCC:TAATTGCGTTGC
HW24D1	T:C::T:CAA:CTA:A:TC:T:TTGACTGGTT:GGAA:AGACTACACAGA
OMZ314	T:C::T:CAA:CTA:A:TC:T:TTGACTGGTT:GGAA:AGACTACACAGA
OMZ409	T:C::T:CAA:CTA:A:TC:T:TTGACTGGTT:GGAA:AGACTACACAGA
ATCC49417	A:C::T:CAA:CTA:A:TC:T:TCGACTGGTT:GGAA:AGACTTCACAGA
6/26	T:C::T:CAA:CTA:A:TC:T:TTGACTGGTT:GGAA:AGACTACACAGA
HG564	A:T::G:---:TGC:G:--:G:AGAAACATAC:AATT:GAGGCGTCTTTG

(19)

381	A-----C-CTGCCGCCGATGCTCCTCAGGGTTTCTACGTATTAGAAA
ATCC33277	A-----C-C:G:CGCCGA:G:TCCTCAG::T:::C::AT:A::A:
BH18/10	A-----C-C:G:CGCCGA:G:TCCTCAG::T:::C::AT:A::A:
HW24D1	G-----C-C:T:CAATAA:G:TCCACAA::T:::T::TT:G::G:
OMZ314	G-----C-C:T:CAATAA:G:TCCACAA::T:::T::TT:G::G:
OMZ409	G-----C-C:T:CAATAA:G:TCCACAA::T:::T::TT:G::G:
ATCC49417	G-----C-C:T:CAATAA:G:TCCACAA::T:::T::TT:G::G:
6/26	AATAGGAGCCGC:A:TGTTAA:A:TCCGAAG::A:::T::CT:G::G:
HG564	AATACGAATT-A:G:TGTAGG:G:---C--::C:::T::GC:G::A:

(20)

381	ATGACTACTCAGCTAACGGTGGAACCTATTCATCCGACAATCCTGTGTGTT
ATCC33277	ATG:CT:CTCA::TAACGGT:G:ACTA:T:A::G::A::C::G:::G:T
BH18/10	ATG:CT:CTCA::TAACGGT:G:ACTA:T:A::G::A::C::G:::G:T
HW24D1	GC--C--:TAC--:TCAGAAT:C:GGTC:A:G::T::T::T::A:::G:A
OMZ314	GC--C--:TAC--:TCAGAAT:C:GGTC:A:G::T::T::T::A:::G:A
OMZ409	GC--C--:TAC--:TCAGAAT:C:GGTC:A:G::T::T::T::A:::G:A
ATCC49417	GC--C--:TAC--:TCAGAAT:C:GGTC:A:G::T::T::T::A:::A:A
6/26	GC--C--:TAC--:TCAGAAT:C:GGTC:A:G::T::T::T::A:::G:A
HG564	GTA:AT:TGAT::AAGCAAC:-G--C:T:G::G::G::C::T:::A:C

Fig.6

(21)

```

381      TATGGCAAACCT-TC--AGAAAAACGGAGCCGACTTGGCGGGAGCCGATTT
ATCC33277 T:T::C::A::-TC--:GA:AA:C::AGCCGACT:GGCGGGAGCC:ATT:
BH18/10  T:T::C::A::-TC--:GA:AA:C::AGCCGACT:GGCGGGAGCC:ATT:
HW24D1  A:A::C::G::GACAA:GC:TG:T::TACTCCTT:GAGTTCTGAG:AAA:
OMZ314  A:A::C::G::GACAA:GC:TG:T::TACTCCTT:GAGTTCTGAG:AAA:
OMZ409  A:A::C::G::GACAA:GC:TG:T::TACTCCTT:GAGTTCTGAG:AAA:
ATCC49417 A:A::C::G::GACAA:GC:TG:T::TACTCCTT:GAGTTCTGAG:AAA:
6/26    A:A::C::G::GACAA:GC:TG:T::TACAGCTT:GAGTTCTGAG:AAA:
HG564   T:T::A::G::GCTCG:TA:GG:C::CAACCCTC:CACGGAACCA:CCT:

```

(22)

```

381      AGCAGCTGCTCAGGCCGCCAATTGGGTGGATGCAG-----AAGGC-AAGA
ATCC33277 AG:A:C:::TCAGGCC:::AATT::G:GGA:::AG-----A:GGC-:A::
BH18/10  AG:A:C:::TCAGGCC:::AATT::G:GGA:::AG-----A:GGC-:A::
HW24D1  GA:A:C:::ATTCAAT:::GGCT::A:TGT:::AGACAATA:TCCT:C::
OMZ314  GA:A:C:::ATTCAAT:::GGCT::A:TGT:::AGACAATA:TCCT:C::
OMZ409  GA:A:C:::ATTCAAT:::GGCT::A:TGT:::AGACAATA:TCCT:C::
ATCC49417 GA:A:C:::ATTCAAT:::GGCT::A:TGT:::AAACAATG:TCCT:C::
6/26    GA:A:C:::ATTCAAT:::GGCT::A:TGT:::AAACAATG:TCCT:C::
HG564   GA:G:A:::TATAAAT:::----:A:T-C:::-GACGGAG:TGGC:C::

```

(23)

```

381      CCTATTACCCTGTATTGGTAAACTTCAACAGCAACAACCTATACTTATGAC
ATCC33277 :C::T::C::T:::G::A:::TCA:CA:::CAAC::T:CT::TGA:
BH18/10  :C::T::C::T:::G::A:::TCA:CA:::CAAC::T:CT::TGA:
HW24D1  :C::T::C::T:::G::A:::TCA:CA:::CAAC::T:CT::TGA:
OMZ314  :C::T::C::T:::G::A:::TCA:CA:::CAAC::T:CT::TGA:
OMZ409  :C::T::C::T:::G::A:::TCA:CA:::CAAC::T:CT::TGA:
ATCC49417 :C::T::T::T:::A::G:::TTG:GA:::TAAT::C:CC::C-A:
6/26    :C::T::T::T:::A::G:::TTG:GA:::TAAT::C:CC::C-A:
HG564   :T::C::T::G:::G::G:::ATG:TG:::TGGC::C:TC::T-T:

```

(24)

```

381      A-GCA--ATTA-T-ACGCCTAAGAATAAAATTGAGCGTAACCATAAGTAT
ATCC33277 :-GCA--ATTA-T-AC:CCT::GA:T:::T:AG::T:::C:TA:G:AT
BH18/10  :-GCA--ATTA-T-AC:CCT::GA:T:::T:AG::T:::C:TA:G:AT
HW24D1  :-ATG--GTTA-T-AC:CCT::GA:T:::T:AG::T:::C:TA:G:AT
OMZ314  :-ATG--GTTA-T-AC:CCT::GA:T:::T:AG::T:::C:TA:G:AT
OMZ409  :-ATG--GTTA-T-AC:CCT::GA:T:::T:AG::T:::C:TA:G:AT
ATCC49417 :GGTG--AGGC-TGTT:AGA:GG:-:::C:TT::T:::C:TA:A:TC
6/26    :GGTG--AGGC-TGTT:AGA:GG:-:::C:TT::T:::C:TA:G:TC
HG564   :GGTGCTATTACCCAA:GAC::-A:C:::C:TT::C:::A:CC:C:AC

```

Fig.7

(25)

381	GATATTAAGTTGACAATTACAGGCCCGGAACGAATAACCCAGAGAATCC
ATCC33277	G:T::T:AGT:::CA::T::A::C::C::A:::AC::A::G::T::
BH18/10	G:T::T:AGT:::CA::T::A::C::C::A:::AC::A::G::T::
HW24D1	G:T::T:AGT:::CA::T::A::C::C::A:::AC::A::G::T::
OMZ314	G:T::T:AGT:::CA::T::A::C::C::A:::AC::A::G::T::
OMZ409	G:T::T:AGT:::CA::T::A::C::C::A:::AC::A::G::T::
ATCC49417	G:C::C:ACC:::CG::C::C::T::T:::AT::T::A::C::
6/26	G:C::C:ACC:::CG::C::C::T::T:::AT::T::A::C::
HG564	A:G::T:CGC:::AC::C::C::C::C::T:::CT::T::A::T::

(26)

381	TATCACAGAGTCTGCTCACTTGAATGTACAGTGCAGTGTAGCTGAGTGGG
ATCC33277	TATCA:A:AGTCT::TC::T:G::T::ACAG::CACT::AG:TGAG:::G
BH18/10	TATCA:A:AGTCT::TC::T:G::T::ACAG::CACT::AG:TGAG:::G
HW24D1	TATCA:A:AGTCT::TC::T:G::T::ACAG::CACT::AG:TGAG:::G
OMZ314	TATCA:A:AGTCT::TC::T:G::T::ACAG::CACT::AG:TGAG:::G
OMZ409	TATCA:A:AGTCT::TC::T:G::T::ACAG::CACT::AG:TGAG:::G
ATCC49417	CATTA:T:AGTCT::TA::C:C::C::TAAT::TGTG::TG:TGCC:::A
6/26	CATTA:T:AGTCT::TA::C:C::C::TAAT::TGTG::TG:TGCA:::A
HG564	TCAAC:G:TACAA::CA::C:G::T::TACT::CCAA::TA:ACCT:::G

(27)

381	TTCTCGTTGGTCAGAATGCTACTTGGTAATCGACCCGTCAAACGACTAAA
ATCC33277	TTCTC:::GGT:::GAA::C::C:::G:::GA:CCG::AAACG:CT:::
BH18/10	TTCTC:::GGT:::GAA::C::C:::G:::GA:CCG::AAACG:CT:::
HW24D1	TTCTC:::GGT:::GAA::C::C:::G:::GA:CC-::AAACG:CT:::
OMZ314	TTCTC:::GGT:::GAA::C::C:::A:::GG:CC-::AAACG:CT:::
OMZ409	TTCTC:::GGT:::GAA::C::C:::G:::GA:CC-::AAACG:CT:::
ATCC49417	AAGGT:::GTA::AAA::T::T:::G:::GA:CCG::AAACG:CT:::
6/26	AAGGT:::GTA::AAA::T::T:::G:::AG:---::---:TC:::
HG564	TTGTT:::AAT::GGC::C::C:::G:::GA:CCG::AAACG:CT:::

(28)

381	AAACTTTCATAGTTTGTCTATATCGGAATACAGGGAGCGGGGTTTCGCTC
ATCC33277
BH18/10
HW24D1
OMZ314
OMZ409
ATCC49417
6/26
HG564

Fig. 8

50

381 M-----VLKTSNSNRAFGVGDDDESKVAKLTVMVYNGEQQEAIKSAENA
 ATCC33277 M-----VLKT:NSN::F:VGDDDES:VA::V::N:EQ::A::SA:N:
 BH18/10 M-----VLKT:NSN::F:VGDDDES:VA::V::N:EQ::A::SA:N:
 HW24D1 M-----VLKT:NPN::F:E--DES:VA::V::N:EQ::A::SA:N:
 OMZ314 M-----VLKT:NPN::F:E--DES:VA::V::N:EQ::A::SA:N:
 OMZ409 M-----VLKT:NPN::F:E--DES:VA::V::N:EQ::A::SA:N:
 ATCC49417 M-----VLKT:NPN::F:NAGDEA:VA::V::K:EQ::A::SA:N:
 6/26 M-----VLKT:NPN::F:NAGDEA:VA::V::K:EQ::A::SV:N:
 HG564 METDATVSFIIK:GEG::V:DGLADA:IT::A::A:QI::G::TV:E:

100

381 T---KVEDIKC-SAGQRTLVMANTGAMELVGKTLAEVKALTTeltaENQ
 ATCC33277 T---:::D:K:-SAGQ:T::M::TGAME:V::T:A::K:::E::AE::
 BH18/10 T---:::D:K:-SAGQ:T::M::TGAME:V::T:A::K:::E::AE::
 HW24D1 T---:::D:K:-SAGQ:T::M::TGEMK:A::T:A::K:::E::AE::
 OMZ314 T---:::D:K:-SAGQ:T::M::TGEMK:A::T:A::K:::E::AE::
 OMZ409 T---:::D:K:-SAGQ:T::M::TGAME:V::T:A::K:::E::AE::
 ATCC49417 T---:::N:K:-SAGQ:T::M::TGGME:A::T:A::K:::E::EG::
 6/26 I---:::N:K:-GAGQ:T::M::TGGME:A::T:A::K:::E::EG::
 HG564 DGVL:::G:P:KSGAN:V::V::H-NYE:T::S:N::E:::S::AE::

150

381 EAAGLIMTAEPKTIVLKAGKNYIGY-SGTGEGNHIEND-PLKIKRVHARM
 ATCC33277 E:AG:::AEPKTIVLKA:K:YI::-S:TGEG:HIEND-::KIK::H:RM
 BH18/10 E:AG:::AEPKTIVLKA:K:YI::-S:TGEG:HIEND-::KIK::H:RM
 HW24D1 E:AG:::AEPVEVTLVA:N:YY::-D:SQGG:QISQDT::EIK::H:RM
 OMZ314 E:AG:::AEPVEVTLVA:N:YY::-D:SQGG:QISQDT::EIK::H:RM
 OMZ409 E:TG:::AEPVDVTLVA:N:YY::-D:SQGG:QISQDT::EIK::H:RM
 ATCC49417 E:AG:::AEPVEVTLVA:N:YY::-D:SQGG:QISQDT::EIK::R:RI
 6/26 E:AG:::AEPVEVTLVA:N:YY::-D:SQGG:QISQGT::EIK::H:RI
 HG564 N:KN:::GKSAAFTIKP:S:HY::PD:TTS:LVSAGT::AVT::H:GI

200

381 AFTEIKVQMSAAYDNIYTFVP--EKIYGLIAKKQSNLFGATLVNADANYL
 ATCC33277 A:TEIK:Q:SAA:D:I:T:V--EK:YG:I:::Q:NL::AT:VNADAN::
 BH18/10 A:TEIK:Q:SAA:D:I:T:V--EK:YG:I:::Q:NL::AT:VNADAN::
 HW24D1 A:TEIK:Q:SPS:V:K:N:A--EN:YA:V:::E:NL::AS:ANSDDA::
 OMZ314 A:TEIK:Q:SPS:V:K:N:A--EN:YA:V:::E:NL::AS:ANSDDA::
 OMZ409 A:TEIK:Q:SPS:V:K:N:A--EN:YA:V:::E:NL::AS:ANSDDA::
 ATCC49417 A:TKIE:T:SQS:A:K:N:A--EN:YA:V:::K:NL::AS:ANNDDA::
 6/26 A:TKIE:T:SQS:A:K:N:A--EN:YA:V:::K:NL::AS:ANSDDA::
 HG564 S:AGVE:N:ATQ:Q:Y:S:N:ADAK:AA:V:::D:KI::NS:VSNTNA::

Fig. 9

250

381 TGS�TTFNĠAYTPANYANVPWLSRNYVA---PAADAPQGFYVLENDYSAN
 ATCC33277 T:SL:TFN:A:T:ANYANVPW:SRNYVA---PAADAPQ:~::~:ND:SAN
 BH18/10 T:SL:TFN:A:T:ANYANVPW:SRNCVA---PAADAPQ:~::~:ND:SAN
 HW24D1 T:SL:NFN:A:S:ANYTHVDW:GRDYTE---PSNNAPQ:~::~:ST:AQN
 OMZ314 T:SL:NFN:A:S:ANYTHVDW:GRDYTE---PSNNAPQ:~::~:ST:AQN
 OMZ409 T:SL:NFN:A:S:ANYTHVDW:GRDYTE---PSNNAPQ:~::~:ST:AQN
 ATCC49417 T:SL:TFN:A:T:ANYTHVDW:GRDFTE---PSNNAPQ:~::~:ST:AQN
 6/26 T:SL:TFN:A:S:ANYTHVDW:GRDYTEIGAAATVNTPK:~::~:ST:AQN
 HG564 Y:VQ:P-A:L:T:DAAGETYE:EASLN---TNYAVGA:~::~:SK:DAS

300

381 GGTIHPTILCVYGKLQKN-GADLAGADLAAQAANWV--DAEGKTYYPVL
 ATCC33277 GGTIH:~::~:VY:~::~:QKN:-AD:AGADLAA:QA:NWV--DAEGK:~::~:
 BH18/10 GGTIH:~::~:VY:~::~:QKN:-AD:AGADLAA:QA:NWV--DAEGK:~::~:
 HW24D1 AG-LR:~::~:VK:~::~:TKHD:TP:SSEEMTA:FN:GWIVADNNPT:~::~:
 OMZ314 AG-LR:~::~:VK:~::~:TKHD:TP:SSEEMTA:FN:GWIVADNNPT:~::~:
 OMZ409 AG-LR:~::~:VK:~::~:TKHD:TP:SSEEMTA:FN:GWIVADNNPT:~::~:
 ATCC49417 AG-LR:~::~:IK:~::~:TKHD:TP:SSEEMTA:FN:GWIVANNDPT:~::~:
 6/26 AG-LR:~::~:VK:~::~:TKHD:TA:SSEEMTA:FN:GWIVANNDPT:~::~:
 HG564 NE-LR:~::~:IY:~::~:LDKD:NP:TEPALTD:IN:GFC--DGDGT:~::~:

350

381 VNFNSNNYTYDSNYTPKN-KIERNHKYDIKLTITGPGTNNPENPITESAH
 ATCC33277 ::FNS:N:T:DSNYTPKN::~:E::HKYD:K:T:~::~:N::~:ITES:H
 BH18/10 ::FNS:N:T:DSNYTPKN::~:E::HKYD:K:T:~::~:N::~:ITES:H
 HW24D1 ::FNS:N:T:DNGYTPKN::~:E::HKYD:K:T:~::~:N::~:ITES:H
 OMZ314 ::FNS:N:T:DNGYTPKN::~:E::HKYD:K:T:~::~:N::~:ITES:H
 OMZ409 ::FNS:N:T:DNGYTPKN::~:E::HKYD:K:T:~::~:N::~:ITES:H
 ATCC49417 ::FES:N:T:TGEAVEKG::~:V::HKFD:N:T:~::~:N::~:ITES:N
 6/26 ::FES:N:T:TGEAVEKG::~:V::HKFD:N:T:~::~:N::~:ITES:N
 HG564 ::YDG:G:I:SGAITQGQN::~:V::NHYK:T:N:~::~:T::~:QPVQ:N

381	LNVQCTVAEWVLVGQNATW	(347, 37587)
ATCC33277	:::Q:T:AE:VL:G:NATW	(347, 37587)
BH18/10	:::Q:T:AE:VL:G:NATW	(347, 37527)
HW24D1	:::Q:T:AE:VL:G:NATW	(348, 38089)
OMZ314	:::Q:T:AE:VL:G:NAT-	(347, 37903)
OMZ409	:::Q:T:AE:VL:G:NATW	(348, 38076)
ATCC49417	:::N:V:AA:KG:V:NVIW	(350, 37911)
6/26	:::N:V:AA:KG:V:NVIW	(353, 38023)
HG564	:::T:Q:TP:VV:N:AATW	(360, 38239)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP94/01687

A. CLASSIFICATION OF SUBJECT MATTER

Int. C1⁶ C12N15/31, C12P21/02, C12N1/21, C07K14/195, C07K16/12,
A61K38/16, A61K39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int. C1⁵ C12N15/31, C12P21/02, C12N1/21, C07K13/00, A61K39/02,
A61K39/40

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE, WPI, WPI/L, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	Journal of Bacteriology, Vol. 170, No. 4, P. 1658-1665; Dickinson, Douglas P. et al.: "Molecular cloning and sequencing of the gene encoding the fimbrial subunit protein of Bacteroides gingivalis"	1-13, 16-20 14-15
Y	JP, A, 2-135096 (Nihon University and another), May 23, 1990 (23. 05. 90), (Family: none)	14-15
X	JP, B2, 5-26471 (Lion Corp.), April 16, 1993 (16. 04. 93), (Family: none)	21-22

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

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"A" document member of the same patent family

Date of the actual completion of the international search

December 14, 1994 (14. 12. 94)

Date of mailing of the international search report

January 10, 1995 (10. 01. 95)

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